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TROPICAL DISEASES BULLETIN

VOL. 42.] 1945. [No. 10.

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Issued under
the Direction of the
Honorary Managing Committee of the
BUREAU OF HYGIENE AND TROPICAL DISEASES,
Keppel Street, London, W.C.1.
(Telephone: MUSEUM 3041)

Price 2/6 Net.] *Entered as Second Class Matter in the U.S.A. Post.* [Annual Subscription 21/-

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BUREAU OF HYGIENE AND TROPICAL DISEASES.

TROPICAL DISEASES BULLETIN.

Vol. 42.] 1945. [No. 10.

SUMMARY OF RECENT ABSTRACTS.*

VIII. TYPHUS GROUP OF FEVERS.

Proteus OX19 type. Vectors: louse and flea.

Louse typhus.

An important contribution to the understanding of the epidemiology of louse-borne typhus has been made by PSHENICHNOV (p. 836). There is no evidence that infection is transmitted hereditarily in lice, but there is strong evidence that lice may acquire infection from infected louse faeces, which contain masses of rickettsiae from the 3rd to the 17th day after the infecting feed. Louse faeces remain infective for only a short period on the human skin and under conditions of high humidity and warmth, but when dry the faeces may be infective for several weeks or months, especially at low temperatures. Human clothing, therefore, may remain infective, and particles of infective faeces may be introduced on to the conjunctiva or other mucous membranes, by the fingers or nails. Some methods used for the disinfection of clothing are not adequate for the destruction of rickettsiae.

In the *Bol. Oficina Sanitaria Panamericana* (p. 834) there is a report on the incidence of fevers of the typhus group in Latin America. MAGALHÃES (p. 843) describes the rickettsial diseases of Brazil, where tick typhus has existed for many years; epidemic and murine typhus are also found.

GEAR *et al.* (p. 739) have reported on the extensive epidemic of louse-borne typhus which has existed since 1941 in the Transkei and which has been aggravated by the poor nutritional condition of the population. They have established the fact that the disease is not of murine origin, and that the symptoms are those usually found in other countries; the rickettsiae isolated have also been shown to be unexceptional. An alum-precipitated vaccine gave promise of success.

An epidemiological survey of typhus in Egypt since 1905 has been made by KAMAL and MESSIH (p. 380), who state that it is much more prevalent in Lower than in Upper Egypt, and that its incidence is chiefly in the rural population. Spread has been associated especially with the congregation of labour forces and their return home; the winter and spring seasonal prevalence is well marked. During the war the incidence has increased, but this increase did not

*The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1944, v. 41. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

take place before workmen were recruited from Upper Egypt. In an account of the clinical features of a large number of cases of typhus in Egypt, the same authors (p. 382) note that the fatality rate, as is usual, was low in early life and high at ages over 55. There was great variation in the type and severity of the symptoms in the different local outbreaks—the rash was present in only 32 per cent. in one outbreak, but in 95 per cent. in another. For details of other symptoms, and of complications, the original abstract should be consulted. The Weil-Felix reaction remained negative at the end of the third week in 14 per cent. of cases, and the authors do not regard this reaction as absolutely diagnostic unless the titre rises to 1–500 ; a skin test with killed *Proteus OX19* is said to be of value. There was no evidence of the existence of " inapparent " cases, or that any outbreak originated from flea-borne typhus.

Brockbank and Whittaker (p. 383) report 10 cases of typhus in British soldiers who had been in contact with Egyptian labourers ; in 6 the diagnosis was confirmed by the rickettsia agglutination test. The authors point out the difficulty of diagnosis in sporadic cases. In an account of the clinical features of typhus in British troops in the Middle East, Crofton and Dick (p. 1012) emphasize the variability of the disease. Many of their cases were of murine origin, the differentiation from the epidemic type being made by the rickettsia agglutination test ; these murine cases were on the whole less severe than the others, but could not be differentiated solely on clinical grounds.

McConn (p. 111) gives an account of an epidemic of typhus in Ireland. The disease was not at first suspected, and diagnoses of bronchopneumonia and influenza were made, though rashes were found when looked for. Two other outbreaks are also mentioned ; all occurred in Galway. The results of rickettsia agglutination tests on some of these patients, and carried out by Stuart-Harris *et al.* (p. 111), suggest that some, at least, of the patients had been infected with *Rickettsia prowazeki*. The findings give presumptive evidence that human cases of typhus can be classified as murine or epidemic by rickettsial tests.

Sancho Lobo (p. 555) refers to an outbreak of typhus in Córdova, and notes that, as so often happens, the first cases were missed, being mistaken for influenza.

Kudicke (p. 660) believes that the apparent infrequency of typhus in young children is not due to immunity against infection, but to resistance by which the attack is modified. Children are attacked as often as adults, but there are more mild infections, often missed. It is not known how far the blood, in these mild attacks, is infective for lice. Records of the epidemic of typhus in Leningrad during the siege also show that children have no special resistance to actual infection, but that the disease is less severe in them than in adults.; Tokarevich (p. 1017) also demonstrates that the incidence in children in Leningrad was relatively high.

Brevdo (p. 660), in discussing the difficulty of early diagnosis in typhus, draws attention to the appearance of a few single haemorrhagic areas in the region of the sacrum or buttocks, or near the scapulae. These may be seen 24 hours before the typical rash, and are due to early trauma of the tissues through lying on the back. By observing them, diagnosis may be made on the third or fourth day, but they may also be seen in scurvy or other haemorrhagic diseases. Yaluff and Verdaguer (p. 385) refer to minute white spots which may be seen along the retinal vessels in typhus. These are said to be absolutely diagnostic, and have been seen in 80 per cent. of one series of cases. Avtsin (p. 201) describes petechial haemorrhages of the conjunctiva in typhus. These are not often seen in life, but may be found after death in persons who have died late in the disease, or as a result of some complication. Their significance is that they justify a diagnosis of typhus, even in the absence of clinical information.

RAETTIG (p. 932) has studied the blood sedimentation rate in typhus; there is much variation.

CIMMINO (p. 26) has found electrocardiographic evidence of damage to the heart in every case studied in the febrile stage of typhus, and in almost every one in the post-febrile stage. Details of the findings are given in the original abstract. The necessity for avoiding effort during convalescence from typhus is emphasized by KUHLMANN and HEINRICH (p. 932) as a result of their electrocardiographic studies.

KILLIAN and OBERTREIS (p. 662) discuss the surgical complications of typhus. These are of two main types: non-specific septic conditions, and the results of the true typhus lesions of blood vessels, chiefly the small arteries. These are discussed in considerable detail, for which the original abstract should be consulted. The authors note also that during the war in Russia, typhus was common as a complication of surgical conditions. In these circumstances diagnosis can be very difficult.

SEIFERTH (p. 933) notes that the majority of patients with typhus have ear symptoms, usually with deafness which is ascribed to a central cause, but of which the prognosis is generally good. Otitis media is not uncommon.

v. STOCKERT (p. 201) gives a list of the mental disturbances which may occur as a result of typhus.

SEGAL and ZASOSOVA (p. 386) point out that second attacks of typhus are by no means rare; immunity in man is far from absolute. Second attacks tend to be milder than first, and the cardiovascular and nervous systems are less frequently affected.

BENHAMOU *et al.* (p. 25) have, with difficulty, been able to infect mice, by the respiratory route, with material taken by sternal puncture from patients with typhus.

SECRET (p. 661) maintains that typhus can be aborted with certainty by the use of convalescent whole blood if this is given within one or two days of the onset. In comment, MEGAW remarks that it would not be safe to assume that the blood of persons in the 8th or 9th day of convalescence is always free from infectivity. [KILLIAN and OBERTREIS (above) make the point that blood may be infective up to 8 days after defervescence.] BÜHLER (p. 742) writes favourably of the therapeutic effect of convalescent blood, especially if it is given in the early stages of the disease; the blood was taken from young, healthy donors not more than 14 days after defervescence.

PFEFFER and GAUWERKY (p. 274) have treated 50 typhus patients with convalescent serum, and compared the results with 100 controls. There seemed to be some indication of benefit from this treatment, as regards fatality rate, length of fever, and incidence of complications, but the differences between the two series are slight. ALWENS and FRANK (p. 274) have been favourably impressed by the results of treatment with convalescent serum, but the evidence on which they base their claims is not given in sufficient detail to permit evaluation. RAETTIG (p. 275) also reports success with convalescent serum and injections of the patients' own blood, but again the evidence given is poor. MEYER (p. 115) quotes evidence which indicates that convalescent serum administered on the second or third day of an attack of typhus has some effect in reducing the death rate; the results, though suggestive, are not statistically significant.

WOLMAN (p. 933) reports, on the whole favourably, on the treatment of typhus with the serum of horses immunized by injections of increasing doses of living rickettsiae from the intestines of infected lice. The serum is administered subcutaneously, and to be effective, must be given early.

URRA (p. 1019) has had considerable success in the treatment of typhus by the method of Daniélopolu, in which intravenous injections of 250–500 cc.

of a solution containing 0·5 gm. chlorine and 6·5 gm. sodium chloride in 1,000 cc. of water were given once or twice daily. The fatality rate was reduced and although the duration of the fever was not affected, there was striking improvement in the neurological manifestations. These cases were treated in Spain.

It is usually thought that lice infected with typhus live only a few days, but MACCHIAVELLO (p. 385) has found evidence that they may live for a month or more.

DAVIS and WHEELER (p. 743) report experiments on powders tested on man for their louse-killing properties; details are given [but these powders have now been superseded by DDT]. DAVIS *et al.* (p. 744) succeeded in reducing almost to *nil* the louse population of the inhabitants of certain Mexican villages, in which typhus was epidemic, by the use of anti-louse powders and a preparation for the head.

DAVID (p. 664) points out the disadvantages of hydrogen cyanide as a fumigant for louse destruction, and mentions several substances on which work is being conducted and which may prove to be useful for this purpose.

Flea Typhus.

PINTO (p. 27) has found typhus in the rats of Lisbon. A strain of pathogenic rickettsia was isolated from a pool of brain tissue from 5 *Rattus norvegicus*.

BERGE *et al.* (p. 664) report cases of murine typhus in man in Tunisia; rickettsiae have also been isolated from the brains of rats in the same neighbourhood.

In the Ruanda-Urundi district of the Belgian Congo NEUJEAN (p. 1014) noticed, in 1939, a steadily increasing number of sera which gave positive reactions to *Proteus OX19* and *OX2*. Rickettsiae were isolated from lice collected from the patients, and from rats, and though the production of orchitis in guineapigs injected with these strains was by no means constant, the author concludes that the epidemic was of murine origin. The disease was of low virulence and was widespread over a large area. JADIN (p. 1015) also has isolated strains of rickettsiae from rats at Coquilhatville in the Belgian Congo, and has shown that the disease *fièvre rouge congolaise* is a form of murine typhus. In this the Weil-Felix reaction with *Proteus OX19* is not always positive, nor are the rickettsiae always orchitic, but they give cross immunity with strains isolated from cases of murine typhus. Lice can be infected *per rectum* with the rickettsiae and thereafter can transmit the infection, but the author states (without giving evidence in support of his opinion) that the vector is the rat flea.

In spite of the fact that it had been stated that fevers of the typhus group did not exist in Madagascar, BAKER *et al.* (p. 29) report 10 cases in Diego Suarez, where the disease is apparently endemic. No animal experiments could be done, so that no opinion on animal reservoir or vector is expressed, but the Weil-Felix test was usually of the *Proteus OX19* type.

J. C. PATEL (p. 118) reports a few cases of typhus in Bombay; the rat flea may have been the vector. In other cases, lice and ticks have been suspected. N. D. PATEL (p. 387) also gives an account of several cases of endemic typhus in Bombay, apparently of murine origin.

YU and YING (p. 25) give an account of 112 cases of typhus in Kunming; the disease was probably flea-borne, and the attacks were mild.

PLOTZ *et al.* (p. 28) have found a considerable number of cases of endemic typhus in Jamaica under circumstances which suggest that transmission is effected by the ectoparasites of rats. The complement-fixation test to an endemic rickettsial antigen was positive in all cases.

CASTAÑEDA (p. 1018) has found evidence which suggests that typhus of murine origin in Mexico may be spread from man to man by the human louse, and considers that *R. prowazeki* and *R. mooseri*, though different in some respects (notably in respect of cross immunity) are in other ways very similar; that they may arise from a single strain; and that strains intermediate between them can be found. The differences between them, therefore, are only quantitative. He advocates a combined vaccine made from animal lung preparations; large doses of this, injected 5–6 times at weekly intervals, have proved satisfactory in laboratory workers.

MAZZOTTI and VARELA (p. 28) have found infection of the murine type in a cat, in Mexico.

BECK *et al.* (p. 1020) have isolated a strain of rickettsia from the brain of a wild rat in California.

BRICEÑO-IRAGORRY (p. 28) notes that there are two forms of typhus in Venezuela—the murine and a type probably similar to Rocky Mountain spotted fever. He (p. 391) has isolated rickettsiae from the brain of a rat (*R. norvegicus*) in Caracas, Venezuela, for the first time.

MACCHIAVELLO (p. 385) has shown that murine typhus is transmitted from rat to rat by *Polyplax spinulosa* and *Xenopsylla cheopis*. He gives a list of bugs, fleas, mites and ticks in which transmission experiments were negative.

SORDELLI *et al.* (p. 388) have isolated strains of rickettsiae from cases of typhus in Argentina; tests in guineapigs failed to show definitely whether they were of the murine type, and in comment MEGAW suggests that rickettsia agglutination or complement fixation tests on the sera of the patients might achieve better results. The same authors (p. 390) have isolated strains from *Xenopsylla cheopis* in the same area and have attempted to determine their type. The results, however, were highly irregular. The rickettsiae were of low virulence to the local guineapigs, which apparently have a high degree of resistance. The report of another outbreak in man (p. 390) again showed that the infection was mild, and the results in animals inconclusive. The authors (p. 391) have isolated strains of rickettsiae from rat lice and from bed bugs collected from the beds of two infected persons.

BEJARANO (p. 388) notes that flea-borne typhus occurs in Santa Fé, Argentina.

MORAGUES and PINKERTON (pp. 557, 558) have found that mice inoculated with a given dose of murine typhus rickettsiae may develop either inapparent illness or fatal disease, depending on the strain of mouse, and the environmental temperature. An inbred strain was more susceptible than three ordinary strains, and an external temperature about that of the human body led to a much lower mortality than temperatures 20–30 degrees (F.) lower. It seems that the mortality rates can be approximately standardized by attention to these factors, and that this may be useful if mice are used in assessment of therapeutic measures. The bearing of these results on typhus in man is discussed. MORAGUES *et al.* (p. 839) report that if penicillin is given to inbred mice infected with murine rickettsiae, and if the injections are commenced soon after infection, there is a favourable effect on the course of the disease. Secondary infection is eliminated, but in animals which die the rickettsial infection is present. It seems reasonable, therefore, that penicillin may be useful in human disease if it is given early. GREIFF and PINKERTON (p. 840) have found that penicillin injected into eggs in which murine rickettsiae are growing will inhibit that growth, but will not necessarily destroy the organisms.

PETERSON (p. 935) reports that in experimental typhus in mice the oral administration of "Forbisen" is moderately successful, and of toluidin blue very successful, in preventing death, but only if administration is started soon after infection.

Tests.

Weil-Felix reaction.—Felix (p. 552) has summed up modern knowledge of the technique and interpretation of the Weil-Felix test. The details cannot be further abstracted, and should be sought in the original, but it should be noted that although a positive result at a titre of 1–100, or 1–200, is usually regarded as the limit in persons not suffering from typhus, in an endemic area the titre in the healthy may be considerably higher. The essential point is that in typhus the titre should show a pronounced rise in the course of tests made at intervals of 48 hours. High titre reactions are given in diseases of moderate severity; low titres are found in severe or very mild cases, though in the latter they may be high. In comment, Megaw gives the arguments in favour of a classification of the typhus fevers by arthropod vector rather than by the Weil-Felix test.

León and Apodaca (p. 21), having tested the reaction to *Proteus OX19* and *OXK* in healthy persons and in cases of typhus, in Mexico, conclude that titres of 1 in 320 or more are diagnostic with *Pr. OX19*, and of 1 in 200 or more with *Pr. OXK*. The antigenic structure of the rickettsiae contains 3 elements—the purely rickettsial element which always predominates, an element common to the rickettsia and *Pr. OX19*, and one common to the rickettsia and *Pr. OXK* which is the least important. The authors therefore see no justification for using the reaction to *OXK* as a basis for the classification of rickettsiae. In comment, Megaw remarks that the diagnostic significance of these tests cannot be stated in terms of arithmetical figures, and that positive reactions at 1 in 25 or 1 in 50 may be diagnostic in persons known previously to be negative. Low titres may be met in very mild or very severe cases.

Gratch (p. 197) has found that in pregnant women, not suffering from typhus, the Weil-Felix reaction with *Proteus OX19* is positive in relatively high titre. He thinks, therefore, that this may provide a simple early test for pregnancy.

Great fluctuations in the Weil-Felix reaction were observed by Gaase (p. 472) in a series of patients convalescent from typhus and tested every 5 days for several months. The effect of food is noted, and the author emphasizes the importance of making repeated tests in fasting patients. The same author (p. 378) reports that there is much variation in the titre of the Weil-Felix reaction in guineapigs given intracardiac injections of *Proteus OX19*, according to the diet of the animals.

Rubinstein *et al.* (p. 659) have used injections of milk in an effort to provoke a positive Weil-Felix test in suspected cases, with some success. On the other hand, Brevdo (p. 660) states that there is little value in this and similar methods.

Noting the variability of the *O* strains of *Proteus X* used for the Weil-Felix reaction, De la Lastra Soubrier (p. 470) states that by careful selection of typical *O* colonies it is possible to maintain suitable strains. He gives directions for the cultivation of these strains. Bridges (p. 554) has contributed a note, which should be read in the original, on the preparation of suspensions for the Weil-Felix test.

Gaase (p. 114) has investigated the thermostability of typhus agglutinins against *Proteus OX19*. The paper is very technical, and the original abstract should be consulted for details.

Zironi (p. 656) discusses the significance of the frequent occurrence of *Proteus X19* in the blood of typhus patients during the early stages of the fever. The antigen common to *R. prowazeki* and *Pr. X19* inhibits the antibodies which normally prevent *Proteus* from invading the blood stream, and thus allows

increased susceptibility to the latter. This antigen may serve as a source of vaccine against typhus [compare FELIX, this *Bulletin*, 1943, v. 40, 230].

Other tests.—STEUER (p. 113) reviews the use of the dry-blood agglutination test in a number of infectious diseases. In relation to typhus, and with *Proteus* as the antigen, this test is regarded by some workers as very useful in that positive reactions are given only with sera which give positive Weil-Felix reactions in dilutions likely to be significant. BARDHAN *et al.* (p. 379) have used the dry blood test in Egypt, and conclude that subjects with typhus always give positive results, but that the reactions may also be positive in conditions other than typhus. In some of their cases the dry blood test was positive when the Weil-Felix was negative; no explanation of this is given.

EYER and BRIX (p. 23) describe a rapid agglutination test in which a dried suspension of *Pr. OX19* stained with methylene blue, on "structureless" paper, is moistened with tap water, and a drop of the blood to be tested is added. Agglutination is easily seen.

LEÓN and APODACA (p. 379) have found a rapid slide test to be of some value in typhus, though not so useful as the standard Weil-Felix reaction.

VORONINAA and MARKOVICH (p. 1022) have devised a precipitin test in which the polysaccharide X-fraction of *Proteus X19*, described by CASTAÑEDA, is used to precipitate with serum. Preliminary work indicates that the test is useful, and it is simpler than the Weil-Felix.

An account of the technique of the complement-fixation test in rickettsial diseases has been given by BENGTSON (p. 738) but this must be read in the original. In working on complement fixation tests, WERTMAN and PLOTZ (p. 659) have found typhus antibodies in commercial dried and frozen complement; the reason for this is probably that some of the guineapigs used for the preparation of complement may have been used in tests of typhus vaccine. Complement of unknown origin should therefore be tested for these antibodies. PLOTZ *et al.* (p.1023) emphasize the help given, in differential diagnosis of fevers of the typhus group, by the use of the complement fixation reaction.

SMORODINTZEFF and FRADKINA (p. 1021) describe a slide agglutination test, which depends on the fact that in the first few febrile days of typhus there is in the blood an antigen which can be detected by the complement fixation test, but which disappears after the 6th–9th day, when antibodies are formed. Details of the technique should be sought in the original abstract, but the test is performed by mixing a suspension of carmine laden with antibody-containing serum, with a suspension laden with serum from the patient. If the antigen is present, agglutination occurs.

EYER and DILLENBERG (p. 657) have compared the Weil-Felix and the rickettsia agglutination tests in normal persons, vaccinated subjects and patients with typhus. The results show that the rickettsia agglutination test does not give as many non-specific reactions in healthy persons, and that it tends to become positive earlier in the disease than the Weil-Felix. The authors claim that a persistently negative rickettsia agglutination test has never been observed in a proved case of typhus. In persons vaccinated and then hyper-immunized by being bitten by infected lice during the preparation of Weigl's vaccine, the titres of both reactions are surprisingly low.

KLIGLER and OLEJNIK (p. 199) have performed the rickettsia agglutination test on patients with murine and with epidemic typhus. The results indicate that the test can effectively differentiate the two diseases. High specific agglutinin titres are found in rabbits after vaccination with murine and epidemic strains. In view of observed differences in antigenic pattern between different strains of the same type of rickettsiae, the authors argue that vaccines should be polyvalent.

LUMMERZHEIM (p. 380) has used the intradermal test of Giroud in a series of cases of typhus. The test involves the skin reaction to injection of mouse lung vaccine, and usually becomes positive about the 9th day, remaining positive for at least one year.

Vaccination.

DING (p. 116) reports a series of controlled experiments in man in which the protective power of various kinds of typhus vaccine was assessed; the subjects were apparently infected 6–8 weeks after having been vaccinated. There was no evidence that vaccination had any influence in preventing attacks, but there was convincing evidence of the efficacy of killed vaccines of the Cox and other types in preventing death. Yolk-sac vaccines in which *R. prowazeki* and *R. mooseri* were mixed were not so effective as those made from *R. prowazeki* alone. [The author was a German storm-troop leader, and the circumstances under which this experiment was made have been the subject of comment in the *Lancet*.]

As a result of observation of cases of laboratory infection with typhus in man, TOPPING (p. 740) states that if the disease occurs in persons previously vaccinated, the Weil-Felix reaction does not reach the high titres found in the unvaccinated, and that the diagnosis may easily be missed because the disease is mild and atypical. He thinks that vaccination may modify the disease so that it is not infective to lice, and may thus break the man-louse-man cycle and therefore help to control epidemics. The strains in use in the laboratory concerned were both murine and classical, but in only 1 of 14 patients was the strain isolated. WOHLRAB and PATZER (p. 741) also make the point that after vaccination, persons who acquire laboratory infections do not seem to be infective to lice. Attacks in the vaccinated are usually mild, and the titre of the Weil-Felix reactions is low. The authors therefore think that vaccination may be an effective means of controlling epidemics.

A series of 4 laboratory infections with *R. prowazeki* is described by LARSEN and LEBEL (p. 555) from Copenhagen. The method of infection was probably from droplets or inhalation of infected dust, or possibly from infective material on the hands; the workers were engaged with mouse lung preparations; three had been vaccinated, but one, who suffered a severe attack, had not. TOKAREVICH and EPSTEIN (p. 1017) show, once again, that typhus immunization by the Weigl method does not provide complete protection, but that the disease in the immunized is mild.

PENFOLD (p. 387) has recorded the *Proteus* agglutination titres of 23 healthy persons before and after vaccination with a Cox vaccine. Titres in general were low, and many of the subjects gave negative results. MEYER (p. 115) has found that after inoculation with the Weigl vaccine the Weil-Felix reaction is rarely positive at titres above 1–50, but that people so inoculated may, if they suffer from fevers other than typhus, show reactions up to 1–200.

MEYER (p. 473) shows that vaccination with the Weigl vaccine has no effect on the Citochol or Meinicke reactions.

PARK and OFFENKRANTZ (p. 471) have found that in persons vaccinated against typhus almost all were negative to *Proteus OX19* within one year. The response of many of these subjects, at some time, to *Proteus OXK* in low titre is probably to be explained by the antigenic composition of the vaccine; in higher titre the *OXK* reaction still remains a valuable diagnostic test for scrub typhus.

OTTO and MAY (p. 663) make the point that the titre of agglutination of rickettsiae in vaccinated animals has no uniform relationship to the immunizing power of different vaccines, and that the relationship of Giroud's dermal reaction to the degree of immunity has still to be proved.

After a description of louse-borne typhus, REGAMEY (p. 200) notes that for the Swiss army the standard vaccine is a mouse-lung, killed vaccine containing a mixture of *R. mooseri* and *R. prowazeki*.

Work on vaccines carried out in S. Africa by BEVAN (p. 835) shows that protection in animals against rickettsiae of tick-borne typhus is much more effective, with the homologous vaccine, than protection against louse- and flea-borne rickettsiae, with the homologous vaccines. Egg vaccines were found to be preferable to those prepared from animals, especially in relation to tick-borne strains. Repeated egg passage was shown greatly to exalt the virulence of all three forms of rickettsiae.

CLAVERO and PÉREZ GALLARDO (p. 24) have maintained a strain of *Rickettsia prowazeki* by egg-yolk transfers for almost two years, during which time 92 passages were made. The strain, typically virulent at first, has become persistently non-virulent for guineapigs and monkeys, but has fully retained its immunizing power. If this strain remains non-virulent but antigenic, and if it is shown to be incapable of transmission from man to man by lice, there is a possibility that it may be the source of an effective vaccine.

BARTH (p. 657) has used a special strain of *Proteus X19* for vaccinating against typhus; his results show that genuine immunity is conferred in three-quarters of the subjects subsequently tested by injection of blood from typhus patients, and that the serum of vaccinated persons possesses power of neutralization.

Proteus OXK type. Vector: mite.

A team of United States investigators, reporting in the *Bulletin of the U.S. Army Medical Department* (p. 841) describe what is known of the epidemiology and clinical course of scrub typhus. They note that penicillin, even in maximum dosage, has had no effect on the course of the disease.

Tsutsugamushi disease has been reported in troops operating in the Far East. AHLM and LIPSHUTZ (p. 745) report on the clinical features seen in 70 cases, for details of which the original abstract should be consulted. The disease constitutes a serious military problem, and prevention is, of course, important. Indigenous [and therefore probably immune] labourers should be used for clearing camp sites, and the authors give advice on other means which may be taken to avoid infection.

MORISHITA (p. 395) discusses the epidemiology of tsutsugamushi disease in Formosa and the Pescadores.

KRONTOVSKAYA (p. 474), in the course of Russian research in rickettsial diseases, states that a disease identified as Malayan typhus is seen in Central Siberia.

Intermediate type. Vector: tick.

CAMERON (p. 208) does not accept the generally held view that there is a marked difference in virulence between the eastern and the western strains of the rickettsia of Rocky Mountain fever. Studies on a large number of cases indicate that there is no significant difference in comparable age groups. The use of immune rabbit serum in the early stages of the disease seems to be of definite therapeutic value.

More cases of Rocky Mountain spotted fever have been reported from New York State by MAILLARD and HAZEN (p. 474), and two cases are reported by RUBENSTEIN and ROWLEY (p. 119) from Massachusetts.

READING and KLINT (pp. 30, 203) report 4 cases of "spotted fever" from Texas; from 2 of these rickettsiae were passaged in guineapigs, and tests in animals indicated that the infection was of the Rocky Mountain type (ANIGSTEIN and BADER, p. 206).

ANIGSTEIN and BADER (p. 205) have inoculated suspensions of ticks (*R. sanguineus*, *A. americanum* and *A. maculatum*), collected in Texas, into guineapigs. Several of the animals reacted with fever, some with scrotal swelling. There is, however, no record of the isolation of rickettsiae.

BUSTAMANTE and VARELA (pp. 394, 844) have shown that the severe fever of the west coast of Mexico, known by various names, is immunologically indistinguishable from Rocky Mountain spotted fever.

GIBBONS (p. 392) notes that 12 cases of Rocky Mountain fever have been reported in Canada. He gives an account of the distribution of various ticks, and states that typical strains of virulent *R. rickettsi* have been recovered from Canadian *Dermacentor andersoni* from Alberta, where fatal human cases have occurred.

SHELLEY (p. 203) reports 5 cases of tick typhus in Tanganyika Territory.

With the knowledge that bats may harbour the tick *Amblyomma cajennense* and on the supposition that they might therefore, if susceptible, be reservoirs of the rickettsiae of tick-borne typhus, MAGALHÃES and ROCHA (p. 31) have investigated the susceptibility of various bats to the local strains. Two species of bats were found to be susceptible to one strain of rickettsia, but two other strains were not able to infect them. The vampire bat was not susceptible.

MAGALHÃES (p. 31) refers to the pronounced neurotropic properties of the rickettsia of tick-borne typhus of the Brazilian type. MEGAW points out that this disease differs in no essential respect from Rocky Mountain fever.

Although rickettsiae of the Rocky Mountain fever type were found to persist for long periods in the tissues of *Ornithodorus rudis*, DAVIS (p. 32) failed to achieve success in a large number of attempts to transmit the infection by the bite of these ticks. The same author however (p. 32) has proved that *O. parkeri* can transmit the infection by bite, and that the progeny of infected ticks can also transmit by feeding. Transmission was effected by larvae, nymphs and adults, and one female was infective 994 days after the infective feed. Offspring to the 4th generation were infective, 1,333 days after the infective feed, in one instance, and fasting for one year did not prevent infectivity. The rickettsiae maintained full virulence. DAVIS (p. 393) notes that *Ornithodorus nicollei* is able to transmit Rocky Mountain and other similar fevers under laboratory conditions; transmission through the egg occurs.

PLOTZ *et al.* (p. 842) describe a complement fixation test by which Rocky Mountain spotted fever can be differentiated from boutonneuse fever. The rickettsiae contain a common antigen, which is soluble in saline, but they also contain insoluble antigens which are specific, and which react (at significant titres) only with homologous sera. The presence of the common antigen, however, indicates the relationship existing between the two diseases.

TOPPING *et al.* (p. 29) show that sera from three cases of sporadic typhus in India, tested by the complement fixation technique of Bengtson, reacted more strongly to an antigen of the Rocky Mountain fever type than to antigens of the epidemic or endemic typhus types. In comment MEGAW urges that this and the rickettsia agglutination test should be used more widely in India to determine the forms of typhus seen there, since other methods of differentiation have not been satisfactory.

ANIGSTEIN and BADER (p. 665) have shown that injection of rabbit serum immune to Rocky Mountain fever rickettsiae, into guineapigs simultaneously with, and at the site of, intradermal injection of infective suspensions of the rickettsiae, will prevent reaction in the animals, but will not prevent development of protection unless the dose of immune serum is relatively large. The same result is obtained if the serum is injected up to 48 hours after administration of the infective material, but not beyond.

Successful treatment of a series of patients with Rocky Mountain spotted fever is reported by BAKER (p. 207) who used for each injection 0·3 gm. neoarsphenamine dissolved in 10 cc. of an aqueous solution of 1 : 1,000 Metaphen. Administration was repeated at intervals of 3 or 4 days.

A formol-phenol preparation of infected ticks (the Spencer-Parker vaccine) has been used with highly satisfactory results in Brazil, where tick-borne typhus is becoming an increasingly serious problem. PIZA (p. 208) recommends that vaccination should be carried out twice during the first year, and repeated once each year afterwards.

Q fever.

A summary of the epidemiology of Australian Q fever is given by DERRICK (p. 558); this can hardly be abstracted further.

PARKER and KOHLS (p. 277) have found *Rickettsiae diaporica* in *Amblyomma americanum* from Eastern Texas.

Bullis fever.

LIVESAY and POLLARD (p. 209) report laboratory work on Bullis fever, which leads them to conclude that it is caused by rickettsiae which may be transmitted by ticks or mites in the Camp Bullis area of Texas. In the first report of this fever (WOODLAND *et al.*, p. 34) the clinical description suggested rather a disease of the dengue group, but the present authors have found small red-stained rods and coccoid bodies in the cytoplasm and nuclei of cells from the spleen and peritoneum of infected guineapigs, when these were stained by Macchiavello's method. There was no cross immunity with other rickettsial diseases.

ANIGSTEIN and BADER (p. 395) have isolated a strain of rickettsia from *Amblyomma americanum*. Immunity tests suggest that this is the infective agent of Bullis fever. These authors (p. 666), in a more complete investigation of Bullis fever, have shown that the infective agent is present in the blood of patients and in *Amblyomma americanum* collected in the area. Infection of animals did not immunize them against Rocky Mountain fever or Q fever, but did so against subsequent infection with patient's blood. The findings in guineapigs closely resembled those caused by mite-borne typhus, and rickettsia-like bodies were found. The authors therefore consider Bullis fever to be a tick-borne rickettsial disease, but note that the symptoms in man may closely resemble dengue; there is no reaction with *Proteus*.

Trench fever.

BERNSDORF (p. 119) gives a general account of trench fever as it was seen in the German army during the war, with a classification of the clinical types. He argues that *prima facie* a rickettsia is not likely to cause a disease with a pronounced tendency to recurrence, and states that no treatment has been found to have any effect. The disease always ends in recovery. REIMER (p. 120) and SKUJA (p. 121) also give detailed clinical descriptions of trench fever.

The neurological features of trench fever are dealt with by ERNST and PORTIUS (p. 559). The range of diseases which can be simulated is apparently very wide.

ECKARDT (p. 277) thinks that the neurological manifestations of trench fever are due to localized myelitis affecting the posterior horns of the spinal cord.

KÜMMERLING (p. 277) shows that there is yet no diagnostic test for trench fever, and that no drug has been found to have any curative effect; there is danger in the use of any habit-forming drug in a prolonged disease of this kind; WINDORFER (p. 561), however, has found Omnadin very useful. HESSE and KREMSER (p. 1024) write of the use of X-rays in the treatment of trench fever.

Studies on Rickettsiae.

WEISS (p. 378) has studied *R. prowazeki* by electron microscopy. The pleomorphism of the organisms was clearly shown. BEGG *et al.* (p. 838) describe certain inclusion bodies found in association with typhus rickettsiae in animals. They discuss their origin.

FIELDING (p. 24) describes a modified Breinl method for staining rickettsiae, and NYKA (p. 835) a method for staining rickettsiae in histological sections.

Charles Wilcocks.

MALARIA.

RODHAIN, J. & VAN HOOF, M. T. Recherches sur l'anophelisme en Belgique (Deuxième communication). [**The *Anopheles* of Belgium (Second Communication).**] *Ann. Soc. Belge de Méd. Trop.* 1943, Sept.–Dec., v. 23, Nos. 3–4, 209–18, 2 maps.

LEVER, R. J. A. W. **The Anopheline Mosquitoes of Melanesia.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, July, v. 38, No. 6, 499–501. [13 refs.]

A note on *A. punctulatus* and its variety *moluccensis*.

HIATT, E. P. & QUINN, Gertrude P. **The Distribution of Quinine, Cinchonine and Cinchonidine in Fluids and Tissues of Dogs.** *J. Pharm. & Exper. Therap.* 1945, Feb., v. 83, No. 2, 101–5.

The fate of administered quinine in the animal body has recently been receiving further attention. CHEN & GEILING [this *Bulletin*, 1945, v. 42, 348] have studied the mechanism of elimination of quinine and atebrin from the circulation and tissues. HIATT [this *Bulletin*, 1945, v. 42, 178] determined the plasma levels of quinine, quinidine, cinchonine and cinchonidine in man following single doses by mouth. The distribution of these four alkaloids in the tissues and fluids of 11 dogs has been studied by the present authors. Some of the animals were anaesthetized with sodium pentobarbital without obviously affecting the results. Solutions of the sulphates of these substances were given intravenously in equivalent doses at such a rate for 1½ hours that a constant level was maintained in the plasma for at least 30 minutes. Animals were killed at various intervals and determinations of the alkaloids made in tissues and fluids. The colorimetric method devised by BRODIE *et al.* (not yet published by the authors) for the estimation of basic organic compounds was used. A description of the method is given in the present paper. It consists essentially in the extraction of the alkaloids with ethylene dichloride followed by reaction of this extract with methyl orange. After removal of excess of the latter the extract is acidified with HCl in absolute alcohol and read in a colorimeter. Comparison with a calibration curve made from data obtained in the same way indicates the amount of base present. In control experiments, determinations indicated that the alkaloids were recovered in the proportion of 90–103 per cent. of the amount added. [No doubt the latter figure represents the error of the method.] After equivalent doses of the four substances it was found that the plasma concentration and distribution in the tissues and fluids of dogs were approximately the same for each. The plasma levels in dogs showed much less variation than those previously obtained for man. The tissue/plasma ratio in cerebrospinal fluid, red cells, brain, bile and skeletal muscle was low; but was high in the case of glandular tissues and lung. The ratios showed little

variation in spite of alterations in plasma levels, thus indicating a rapid attainment of equilibrium between plasma and tissues. It is probable that the balance would be altered in different animals as the result of variations in the metabolic breakdown of the alkaloids. *J. D. Fulton.*

BROWN, J. S. **Soft Tissue Calcification Secondary to Therapeutic Quinine Injection.** *Brit. J. Radiology.* 1945, June, v. 18, No. 210, 183–4, 5 figs.

Calcified " cysts " in the gluteal regions, discovered as an incidental finding during X-ray examination, are considered by the author to have been caused by therapeutic quinine bihydrochloride (9 gm. in 2 cc. of water) injection. These " cysts " were seen in European or Indian patients only ; African natives were curiously unaffected. They give no trouble, but can often be detected by palpation.

The radiological characters of these calcified masses were sufficiently characteristic to enable the diagnosis to be made solely on the radiograph.

Diagnostic features are :—

(*a*) They occur in the gluteal regions.

(*b*) They are oval in shape, often with a " tail " of calcification along the needle track.

(*c*) They have a mottled consistency.

The author points out that this type of calcification may be seen in soldiers returning from the tropics. [They should not be confused with other types of calcification due to the worm infestation.] *Eric Samuel.*

LANCET. 1945, June 2, 687–9. **Indirect Determination of Plasma Mepacrine in Subjects on a Suppressive Regime. Method suitable for a Field Laboratory.** [Army Malaria Research Unit, Oxford (MAEGRAITH, B. G., *et al.*).]

As recorded in an earlier communication [this *Bulletin*, 1945, v. 42, 251] it has been found that under certain conditions which are discussed below

$$PM = K \times \frac{UM}{UNH_3}$$

where PM is the plasma mepacrine concentration in microgm per litre, UM is the urinary mepacrine concentration in mgm. per litre, UNH_3 is the urinary ammonia-nitrogen in mgm. per 100 cc. and K is a constant. The urinary mepacrine concentration can be measured by the method of KING and GILCHRIST [below]. The urinary ammonia may be measured either by the formol titration method (COLE, 1933) or is a method depending on permutite base-exchange, followed by nesslerization (FOLIN and BELL 1917). Permutite is added to neutral or weakly acid urine and it takes up ammonia ; the supernatant fluid is removed, the permutite is made alkaline, and the ammonia is again liberated into solution and can be estimated colorimetrically by adding Nessler's reagent. The figure given for ammonia by the formol titration method is 20 per cent. higher than that by the other method.

Ten subjects were used for the tests, and four observations were made on each. They had been on a suppressive régime of 0·1 gm. mepacrine daily for at least six weeks. They were given 500 cc. of water, and samples of urine were collected at intervals of an hour. The mean value for the constant K in the above equation was 500 when ammonia was measured by formol titration and 420 when it was measured by base exchange. It is recommended that the measurements on the urine should be done in duplicate, and that the mean value should be used for the calculation.

When direct estimations were made of the plasma mepacrine, the standard deviation of the mean of triplicate estimations was $\pm 4{\cdot}1$ microgm. per litre ;

the values of the mean ranged from 10 to 36 microgm. When the plasma mepacrine was calculated from the observations on the urine the standard deviation of the mean error (*i.e.* error of urinary field analysis plus errors inherent in the biological relation expressed in the equation) was ±4·0 microgm. per litre if the formol titration method was used, and ±5·6 microgm. per litre if the base-exchange method was used. The mean error is measured by the difference between the value obtained by direct examination of the plasma and that obtained by calculation from the urine. In view of the simple methods employed, the errors of the indirect method are remarkably small. This equation, however, is correct only for men who have been on suppressive mepacrine for at least six weeks. For other régimes of mepacrine administration it is necessary to calibrate the equation to suit that particular régime, by making a series of direct measurements of plasma mepacrine and comparing them with the concentrations of mepacrine and ammonia in the urine [see BROWN and RENNIE below]. *F. Hawking.*

ANN. TROP. MED. & PARASIT. 1945, May 31, v. 39, No. 1, 53–60, 1 fig. **Factors affecting the Excretion of Mepacrine in the Urine.** [Army Malaria Research Unit, Oxford (MAEGRAITH, B. G., *et al.*).]

The first part of this paper describes in greater detail the observations which led to the conclusion that the relation between plasma mepacrine, urine mepacrine, and urine ammonia could be expressed by the above equation

$$PM = K \times \frac{UM}{UNH_3}$$

Nine volunteers who had been on suppressive mepacrine (0·1 gm. daily) for some weeks were given ammonium chloride or sodium bicarbonate, to make the urine acid or alkaline respectively. It was found that although the dosage of mepacrine remained constant, the excretion of mepacrine was much greater (up to 10 times as great) when the urine was acid, than it was when the urine was alkaline. In general, the mepacrine output increases as the *p*H decreases. The relation between urine mepacrine output and titratable acidity was fairly close, but not so close as that between the urinary output of mepacrine and the urinary ammonia.

Plasma mepacrine (microgm. per litre)=151 urinary output of mepacrine (mgm. per hour)—73 urinary output of ammonia (mgm. nitrogen per hour) +20·3, but the equation $PM = K \times \frac{UM}{UNH_3}$ is easier to use since it involves the concentrations in the urine and not the volume of urine, and it is practically as accurate.

Reference is made to the paper of BROWN and RENNIE [below], and it is emphasized that the above equation holds only for men who have been on suppressive mepacrine for some weeks. At an E.M.S. hospital six patients were studied who had received a therapeutic course of mepacrine. The concentration of mepacrine in the plasma was calculated from estimations of urinary mepacrine and ammonia by means of the first equation given by BROWN and RENNIE. The results were in fair agreement with those obtained by direct examination of the plasma; in 3 patients the agreement was very close, in 2 patients the indirect estimate was 40–48 per cent. too high. *F. Hawking.*

BROWN, M. & RENNIE, J. L. **Indirect Determination of Plasma Mepacrine during a Therapeutic Course.** *Lancet.* 1945, June 2, 686–7, 2 figs.

Observations were made on the relation between plasma mepacrine on the one hand, and urine mepacrine and urine ammonia on the other. These

observations were made in 35 patients who had received a therapeutic course of mepacrine, 0·2 gm. four times daily for 2 days and then 0·1 gm. thrice daily for 4–10 days. The specimens of plasma and of urine were collected 12–15 hours after the last tablet had been administered. The urine ammonia (UNH_3) was measured by formol titration in mgm. per 100 ml. The plasma levels of mepacrine (PM) ranged from 14 to 75 microgm. per litre, and the urinary mepacrine (UM) concentrations ranged from 1·3 to 19·3 mgm. per litre. Under these conditions

$$PM = \frac{UM}{UNH_3} \times 109 + 27$$

or a better fit for the data was given by the equation

$$PM = 2{\cdot}36\ UM - 0{\cdot}42\ UNH_3 + 47.$$

Further observations were made on 51 patients, admitted to hospital with malaria, who had taken suppressive mepacrine irregularly for as long as five months. The plasma mepacrine concentrations ranged from 0 to 35 microgram per litre, and the urinary mepacrine concentrations ranged from 0·03 to 2·50 mgm. per litre. For these patients, PM=7·3 UM+4.

Another series of observations was made on 36 patients who had finished the above therapeutic course of mepacrine. The plasma mepacrine concentrations ranged from 12 to 100 microgram per litre, and the urinary concentrations of mepacrine from 0·9 to 17·0 mgm. per litre. For these subjects PM=1·5 UM+28. Clearly the dosage of mepacrine used has a strong influence on the relation between the concentration of mepacrine in the plasma and that in the urine. The authors emphasize that the laboratory manipulations for the indirect method of estimating plasma mepacrine by urinary examination are far simpler than those required for direct estimation by examination of the plasma. But they repeat that it is necessary to work out the relevant equation of prediction by parallel direct determinations on a sample of the group involved. [In view of the fact that four different equations have been given for four different groups of subjects, this working out of the equation for each particular context certainly seems essential. The necessity for this preliminary investigation greatly diminishes the advantages claimed for the simplicity of this indirect method of measuring plasma mepacrine.] *F. Hawking.*

King, E. J. & Gilchrist, Margaret. **Field Method of estimating Mepacrine in Urine.** *Lancet.* 1945, June 2, 686.

The method makes use of a Lovibond All-Purposes Comparator or Nessleriser fitted with special mepacrine discs ranging from 0·5–5 mgm. per litre (obtainable from Tintometer, Ltd., Milford, Salisbury, or from British Drug Houses, Ltd.).

" To 50 ml. of urine in a separating funnel, add 2 ml. of 10 per cent. NaOH and about 100 ml. of ether or paraffin. Shake well, allow to separate, and drain off as much of the urine layer as possible. Wash by shaking with 10 ml. of 10 per cent. NaOH and draining off. (The shaking and separating can be done in medicine bottles, by decanting and sucking off, but a separating funnel is more convenient.) If the colour is to be read in the Comparator, add 18 ml. N HCl ; if it is to be read in the Nessleriser, add 50 ml. of N HCl. Shake well, allow to separate, and drain off as completely as possible into the 4 cm. Comparator cells or the Nessleriser tubes. Compare with coloured disc. If globules of ether or paraffin remain suspended in the HCl extract and make the reading of the colour difficult, the extract should be passed through a filter paper.

" If the colour is too strong, dilute 1 : 1 with N HCl and read again.

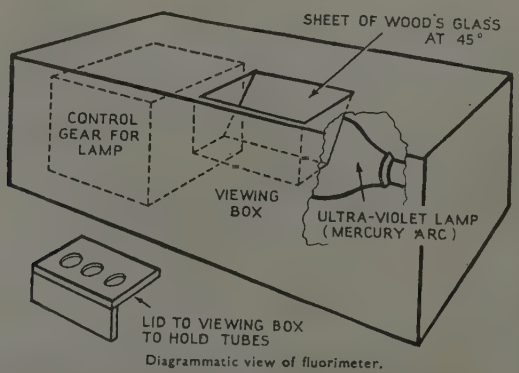
" If the colour is too weak (*i.e.*, less than 0·5 mg. mepacrine per litre), 100 ml. (or 200 ml.) of urine should be extracted with the 100 ml. of ether or paraffin

in a 500 ml. separating funnel. The mixture should not be shaken violently lest an emulsion form ; it is sufficient to mix well by gentle inversion (about 1 a second) 30 or 40 times. The rest of the procedure is the same as above, and the result is divided by 2 (or 4)." *F. Hawking.*

King, E. J. & Gilchrist, Margaret. **Field Method for Direct Estimation of Mepacrine in Plasma and Blood.** *Lancet.* 1945, June 30, 814, 1 fig.

" In a separating funnel are placed 10 ml. of 0·3N.NaOH, 25 ml. of petroleum ether, and 25 ml. of the isopropylisobutyl alcohol mixture [redistilled isopropyl and redistilled isobutyl alcohol, equal parts] ; 5 ml. plasma (potassium-oxalate or citrate, or heparin), or 5 ml. whole blood is added and the mixture shaken vigorously for 1 min. and then allowed to separate. The blood layer is discarded. The mixture is washed with 10 ml. of 0·3N.NaOH by shaking vigorously for 1 min., and the NaOH discarded. The NaOH wash is repeated twice and the NaOH layer separated as completely as possible. The mepacrine is next extracted into 5 ml. of the acid alcohol mixture by shaking vigorously for 1 min. After it has separated out, the acid layer is run off into a centrifuge-tube and spun clear. 4 ml. of the clear solution is pipetted into a non-fluorescent test-tube. Alkaline borate buffer (1 ml.) is added, and the green fluorescence compared with standard solutions freshly prepared by dilution with acid alcohol from the stock standard, and treated with alkaline borate buffer in the same manner as the unknown. The fluorimeter requires about 10 min. to warm up and should be used in the dark.

" The standard mepacrine solution contains 100 mg. per litre. [It is made by dissolving one 0·1 gm. tablet of mepacrine in one litre 0·1 N.HCl. It should be prepared monthly and kept in the dark.] A dilute standard solution is prepared by diluting 10 ml. of the strong standard to 1 litre with 0·1N.HCl. This solution should be prepared freshly for use. Fluorescent standards are prepared as follows : 0·1 ml., 0·2 ml., 0·4 ml., 0·8 ml., and 1·2 ml. dilute standard are each diluted to 5 ml. with the acid alcohol mixture ; 4 ml. of each of these is treated with 1 ml. NaOH-borate buffer. These are equivalent to 20μg., 40μg., 80μg., 120μg., and 240μg. per litre respectively. Additional standards of intermediate strengths may be prepared if it is desired to match the blood strengths more closely. For very high mepacrine concentrations, 2 ml. of whole blood may be used instead of 5 ml. For very low plasma concentrations, 10 ml. should be used instead of 5 ml.


SHEET OF WOOD'S GLASS AT 45°
CONTROL GEAR FOR LAMP
VIEWING BOX
ULTRA-VIOLET LAMP (MERCURY ARC)
LID TO VIEWING BOX TO HOLD TUBES

Diagrammatic view of fluorimeter.

[Reproduced from the *Lancet.*]

" The fluorimeter (see figure) is used on a 220–240 volt AC circuit. It should be turned on about 10 minutes before use. The blood fluorescent tube is placed between two standards for matching. The tubes may be viewed vertically, by placing them in the holes of the rack provided, or they may be viewed horizontally by removing the rack and placing the tubes in the well. Once the lamp has been switched off, it must not be used again until it has cooled down. It should, therefore, be kept on continuously until each set of matchings has been completed. Suitable lamps are the ' Osira ' 80 watt black glass lamp, 230 volt, with choke, as GEC leaflet 05 7196, or Philips's MBW–V ' Philora ' ultraviolet mercury lamp with lampholder and choke. The whole apparatus, in a convenient assemblage and readily portable form, may be obtained from the Tintometer Ltd., Milford, Salisbury, at an approximate cost of ten guineas." *F. Hawking.*

HENRY, A. J. & GRINDLEY, D. N. **The Adsorption-Fluorescence Estimation of Mepacrine and Stilbamidine.** *Ann. Trop. Med. & Parasit.* 1945, May 31, v. 39, No. 1, 1–7. [11 refs.]

Various improvements are described in the method devised by the authors for estimating stilbamidine in urine [this *Bulletin*, 1943, v. 40, 122]. Briefly this method consists of dropping small volumes of the fluid under test on to filter paper, drying, and comparing the fluorescence under ultra-violet light with that produced by known concentrations of the compound. In the new technique a graduated 1 cc. pipette is drawn out to fine capillary point, with a right-angle bend 1·5 cm. above the end of the capillary. The pipette is filled with fluid and clamped horizontally, the capillary end being in light contact with a filter paper. Fluid is allowed to run out slowly on to the filter paper so that there is very little free liquid on the paper at any one time. Altogether 1 cc. of fluid may be used. The stilbamidine present is adsorbed on to the filter paper. A small amount of water (0·2 or 0·3 cc.) is then run through the pipette on to the filter paper in the same way, to wash out urinary pigments or quinine. The paper is then dried and the fluorescence measured by comparison with standard papers any time during the next half year. By this technique stilbamidine may be detected in concentrations down to 0·02 mgm. per 100 cc. [lower concentrations can probably be detected if a powerful lamp, condenser, and Wood's glass filter are used]. Mepacrine can be measured in urine by the same technique, the range being from 0·25 mgm. to 10 mgm. per 100 cc. in the original urine; the accuracy is not very high. The application of this method is illustrated by the measurements of the mepacrine excreted in the urine of a patient treated for malaria. [This method is very simple and convenient for the estimation of stilbamidine; for the estimation of mepacrine the method of KING and GILCHRIST, above, is more accurate and more sensitive.] *F. Hawking.*

BUTT, H. R., HALL, J. E., WATKINS, C. H. & CRAGG, R. W. **Atabrine Dihydrochloride (Quinacrine Hydrochloride); some Observations on its Toxicity and on its Use in the Treatment of Malaria with particular reference to its Effect on the Liver.** *Gastroenterology.* 1945, Mar., v. 4, No. 3, 205–12. [17 refs.]

Fifty young men were studied who had suffered from multiple relapses of malaria [presumably due to *P. vivax*]. They had not received mepacrine for at least 2 weeks before this study was made, and all but one were free from demonstrable malaria parasites at the time when observed. They were given 4·5 gm. mepacrine in 10 days by mouth, 0·8 gm. being given on the first day.

Liver function tests were carried out at the end of the ten days. In 48 of the men, a bromsulphalein test was done ; at the end of the ten days the test was normal in all but one (a man who had a 6–12 per cent. retention of the dye). The prothrombin time, serum bilirubin, haemoglobin estimation, erythrocyte, leucocyte, and differential counts were all within normal limits, and so were special smears for macrocytosis. No significant changes occurred in the van den Bergh reactions, many of which were positive before treatment began, or in the urine. Staining of the skin was clinically demonstrable in 18 of the subjects. Mild gastro-intestinal or other symptoms, especially diarrhoea, occurred in 21 of the patients, but their significance is doubtful. Since all these men had suffered from liver damage during their previous attacks of malaria, and 13 had had clinical jaundice, it is noteworthy that no significant signs of liver damage due to mepacrine were discovered in them following this course of treatment. [This conclusion agrees with the results obtained at the Royal Army Medical College and in other military research units during the present war.] *F. Hawking.*

Berry, J. N. **Two Cases showing Cerebral Symptoms after Treatment with Quinacrine for Malaria.** *Indian Med. Gaz.* 1945, Apr., v. 80, No. 4, 214.

Hegsted, D. M., McKibbin, J. M. & Stare, F. J. **The Effect of Atabrine on Thiamine Deficiency in the Young Rat.** *J. Nutrition.* 1945, May 10, v. 29, No. 5, 361–3, 1 fig.

In previous experiments [this *Bulletin*, 1944, v. 41, 649] the influence of modifications of certain diet on the toxicity of atabrine [mepacrine] for young rats was investigated, and atabrine was shown to have a " choline-like " or " choline-sparing " action ; further experiments are recorded in the present paper.

The same diet was used except that thiamin was omitted ; the diet was given to 36 young male rats and 18 of them received also atabrine hydrochloride with the food—40 mgm. per 100 gm. of ration. " After 13 days the animals not receiving atabrine began to lose weight ; they were then divided into six groups and fed thiamin supplements." The results are shown in the table :—

Group	Atabrine mgm.%	Weight at end of depletion period, gm.	Thiamin µgm.	Gain in 30 days, gm.	Gain of atabrine groups compared to control, %
1	0	17·0	3	7·5	
2	40	18·5	3	23·8	318
3	0	18·5	6	36·0	
4	40	16·0	6	50·0	139
5	0	24·8	9	60·4	
6	40	19·2	9	54·4	90

The experiment was repeated with the food consumption equalized in the control and the atabrine groups, with a similar result ; it was again repeated with equalized food intake, giving the basal ration only as the diet, and was continued until the rats died. The life of the atabrine rats averaged 43 days, that of the controls 25 days ; the former showed severe polyneuritis, the latter not, as they died before such symptoms developed.

It was concluded that atabrine has a thiamin-sparing action.

J. F. Corson.

McCoy, C. R. **Suppressive Treatment of Malaria in Military Forces.** *J. National Malaria Soc.* Tallahassee, Fla. 1945, Mar., v. 4, No. 1, 9–12.

Extensive war experience has amply demonstrated the value of atebrin [mepacrine], 0·1 gm. daily, for suppression of malaria. It is much more effective than quinine, is better tolerated and preferred by troops. Many thousands of troops have taken atebrin in these doses for periods longer than a year with no evidence of toxic effects. Symptoms suggestive of intolerance—nausea, vomiting, and occasionally abdominal cramps and diarrhoea, which may appear after one or more of the first few doses—are never serious and soon disappear if the drug be continued. True intolerance has rarely been observed. The maximum plasma concentration of the drug on a given dosage is not attained until after four to six weeks. In *falciparum* malaria atebrin in the above dosage not only prevents clinical attacks but also, if it be continued for four weeks after the last exposure to infection, cures the disease. Atebrin will not, however, prevent relapses of *vivax* malaria after the medication ceases. It may be necessary to continue suppressive treatment after exposure to infection has ceased in order to maintain military effectiveness. No evidence has appeared that long continued administration of atebrin produces drug resistant strains of plasmodia. The effectiveness of atebrin suppression tends to conceal the rate at which malaria infection is being acquired and may thus lead to neglect of antimosquito measures ; this must be guarded against. The use of atebrin has been a very great help to military forces but it must not be regarded as a solution to the malaria problem. *Norman White.*

Symes, C. B. & Hadaway, A. B. **Report on the Initiation of certain Experiments on the Use of D.D.T. for the Control of Malaria in British Guiana.** 81 mimeographed pp. 1945. July 17.

The authors arrived in British Guiana in January 1945, and, in consultation with Dr. Giglioli and Dr. Bevier, chose two sugar plantations and one rice-growing area for their experiments. In these places malaria is hyperendemic and filariasis is common. The most important vector of the former is *Anopheles darlingi*, which breeds in canals, drains and other surface waters, and which is domestic in its habits ; it breeds throughout the year. Rainfall is heavy during the whole year (94 inches in Georgetown), but there are " wet " seasons ; during these there is breeding of *A. aquasalis* and *A. albitarsis*, but they are not important vectors. *Culex fatigans* is very common.

In the various places in which the experiments were carried out, examinations for malaria were made on the children, and information was collected on the mosquito population.

The labourers on the sugar plantations live in quarters (known as ranges) which consist of blocks of 10 rooms with a verandah (gallery) along one side of the block. DDT was applied to certain rooms in the test ranges after a study of the mosquito population had been made, and the results were compared with those of control rooms in unsprayed ranges.

The solution used was 4·6 per cent. DDT in kerosene, and the calculated dosage actually applied to walls, roofs, etc., was 2·05 quarts per 1,000 square feet—approximately 106 mgm. crude DDT per square foot. The results of one application were judged by captures of adult mosquitoes made in the rooms during several weeks. In one area (Lusignan) the reduction in captures of all species amounted to 95·9 per cent. of the control captures as late as the 7th week after the application. Evidence accumulated throughout the investigation that the effect of DDT is much greater on *A. darlingi* than on *C. fatigans*.

In the second area the verandahs of the ranges were treated, in addition to the rooms ; the results were again very satisfactory for several weeks. In the

third area, where rice cultivation was carried out and where the people lived in small houses of wood, mud and thatch, or with "iron" roofs, DDT was used as a 5 per cent. solution in hydrocarbon oil and kerosene, as a 2½ per cent. solution, or as a 5 per cent. emulsion. Again the results were good as regards *A. darlingi*, but not so good with *C. fatigans*. The weaker solution "seems to be roughly as effective as the 5 per cent. solution and emulsion over a four week period. It remains to be seen from later observations how its toxicity will last." Mud walls, thatched roofs and painted or whitewashed wood seem to have reduced the efficiency against *C. fatigans*; the reason is not clear.

At Lodge village 67 gallons of a 7 per cent. emulsion were discharged into the open air as a fine mist from a Hochberg-Lamer generator. The facilities for mosquito breeding were abundant, and it was found that at least 3rd and 4th stage anopheline larvae were killed to a distance of about 2,000 feet from the generator, and probably further. First and second stage larvae (probably new hatchings) were found 48 hours after treatment. High rates of kill of adult mosquitoes were obtained in houses fairly close to the generator, but 4,000 feet away the kill was only 18 and 52·3 per cent. respectively in two areas. The method holds promise of success, but research is needed in various directions.

There is much investigation still to be done, and the authors make specific mention of many of the points which need elucidation, in particular of the need to study the behaviour of solutions and emulsions, in various vehicles, on the different materials used in building. They make the point that hand catching is a poor method of estimating residual mosquito populations, and that better results are obtained after the use of a pyrethrum spray.

An interesting observation is that *A. darlingi* frequents ground shaded by vegetation during the day-time, and that spraying of the vegetation would probably not be successful in dealing with it unless the ground also were sprayed. The authors discuss in detail the types of sprayers tried in their work, and the solvents used.

Complete tables of results are given, in great detail; the original report should be consulted by those who are engaged on similar work.

Charles Wilcocks.

GILROY, A. B. & CHWATT, L. J. **Mosquito-Control by Swamp Drainage in the Coastal Belt of Nigeria.** *Ann. Trop. Med. & Parasit.* 1945, May 31, v. 39, No. 1, 19–40, 3 maps, 4 text figs. & 7 figs. on 4 pls.

A full description is given of the rationale, technique, and results of draining mangrove swamps in the vicinity of Lagos for the protection of Service personnel from malaria. There is a difference of about two feet between the normal and the maximum high tides, and in consequence there are three main coastal zones of vegetation with different characteristics; a low-lying swampy foreshore, fringed with a belt of *Rhizophora* mangrove, 20 to 400 feet wide, exposed to all tides and not affording mosquito breeding places; a more or less open sandy shore only reached by high tides, where there may be swamps, covered with marsh grass, and *Avicennia* mangrove, with many crab holes and shallow pools, which constitute the main breeding places of *Anopheles melas*; and relatively high land above the reach of spring tides, covered with a dense growth of low bush, providing occasional breeding places for *Anopheles gambiae* and other anophelines in casual rainwater pools. The object of swamp drainage is to provide an embankment on the seaward side of the second zone, to prevent access of high tides, and to drain the land above the embankment to a low level channel inside it, and thence through one-way tide gates to the sea. The important second zone is thus dried out and most anopheline breeding comes to an end.

The low level drain and the embankment are made simultaneously, the soil from the one being used for the other, about 50 to 60 feet inland from the shore. Tide gates in a standard concrete framework, of which detailed plans are given, are then inserted in the embankment, the sill being about 3 feet below mean sea level, after which such main, contour and subsidiary drains as are necessary are constructed in the area enclosed. The embankment must be made good from time to time, to remedy the effects of subsidence and wave action, and the more vulnerable parts may be protected by a thin concrete facing. Tide gates cost £200 each, and the total cost of reclamation amounted to £18 6s. per acre, 1,700 acres having been reclaimed by a labour force which varied between 700 and 800 ; 1,300 acres were reclaimed in one year.

The reclaimed area dries out very rapidly, though occasionally low parts may need filling from neighbouring higher ground. Mosquito breeding in the *Avicennia* and marsh grass swamps ceases within a few days of completion of work, and drainage channels remain free of larvae owing to the presence of numerous larvivorous fish. The work was followed by a marked fall in anophelines in nearby catching stations and in the malaria rate, though credit must be shared between this drainage and the removal of the local population of gametocyte carriers, following which the sporozoite rate of *Anopheles gambiae* dropped from 4·8 to 1·3 per cent. Experiments have been made in the use of the reclaimed land, and reafforestation with *Melaleuca* and *Casuarina* species has been found possible, data being presented on the results with these and other tree species.

[The paper is a useful contribution to our knowledge of control of *A. melas*, and should be studied in the original by anyone undertaking work of this nature.] *G. Macdonald.*

THOMPSON, P. E. **The Effects of Sulfonamide Diets upon Infections of *Plasmodium elongatum* in Canaries.** *J. Infect. Dis.* 1945, Jan.–Feb., v. 76, No. 1, 15–19.

Though, in common with a number of malarial parasites of birds, *P. elongatum* reproduces by exoerythrocytic as well as by erythrocytic schizogony, it is peculiar in that the exoerythrocytic development occurs not in cells of the macrophage or endothelial type but in various blood and blood-forming cells. As COGGESHALL, PORTER and LAIRD [this *Bulletin*, 1945, v. 42, 699] have shown that sulphadiazine and sulphapyrazine are able to eradicate exoerythrocytic forms of *P. gallinaceum*, it seemed to the authors advisable to test the action of sulphonamides on the different exoerythrocytic forms of *P. elongatum*. In the tests carried out in canaries the drugs were administered in the food, a special mixture having been devised which was sufficiently attractive to the birds to ensure that a fairly regular daily dosage was consumed. It was found that when the concentration of the sulphadiazine in the food was 1·3 per cent., blood levels ranging from 15·1 to 26·4 mgm. per cent. were obtained. With a food concentration of 0·65 per cent. of sulphapyrazine, blood levels of 12·8 to 20·3 mgm. per cent. resulted. It was found that food containing 1·3 per cent. sulphadiazine had no influence in the exoerythrocytic stages. The result was the same when the food concentration of sulphadiazine was raised to 2 per cent. and when food with 0·65 per cent. sulphapyrazine was used instead. When treatment was commenced before inoculation of parasites, both drugs had some suppressive action on the infection. *C. M. Wenyon.*

BLACKWATER FEVER.

BULL. U.S. ARMY MED. DEPT. 1945, Feb., No. 85, 29–30. **Fluid Intake after Hemolytic Transfusion Reaction.**

Patients with injury of the kidney tubules are not infrequently " harmed rather than helped by peristent efforts to secure diuresis by maintenance of fluid intake in excess of fluid output." It has been shown that " the patient with anuria tends to develop a marked plethora with a circulating blood volume far above the values for normal. Secondly, clinical and pathologic evidence indicate that pulmonary edema is an important cause of death."

Anuria after intravascular haemolysis is due mainly to injury to the epithelium of the renal tubules, and obstruction of the lumen of the tubules by haematin crystals is of secondary importance.

The best time to give diuretics is immediately after the onset of haemolysis. Two measures are recommended: (1) intravenous administration of one litre of isotonic 2 per cent. solution of sodium sulphate within a few minutes after the diagnosis has been made (successive signs are a sense of heat in the skin, headache, a sense of constriction in the chest, rigor, and fever); (2) " fluid administration in excess of output by as much as 3,000 cc. *only* during the first twenty-four hours and mainly during the first twelve hours. *Thereafter, fluids are given strictly in accordance with demands of fluid loss.*

" *The danger of persistent administration of fluids in excess of output are apparent regardless of the cause of anuria or obliguria* " [oliguria ?].

J. F. Corson.

MAEGRAITH, B. **Traumatic Anuria.** [Correspondence.] *Lancet.* 1945, July 14, 58.

Referring to PARAMORE's letter [this *Bulletin*, 1945, v. 42, 452] as a timely warning against the danger of giving too much fluid intravenously in cases of anuria, the author quotes from an article in the *Bulletin of the U.S. Army Medical Department* [above], and suggests that the treatment recommended in that article should be used in Britain in anuria due to blackwater fever, crush injury, and allied conditions. He disagrees with PARAMORE's statement that " whether the first or second convoluted tubules are the more affected can be neglected; however it be, resolution of this question helps neither in prophylaxis nor in treatment ", but, on the contrary, he thinks that investigation of the nature and site of the lesion may lead to knowledge of what the lesion is and how it is produced. *J. F. Corson.* "

TRYPANOSOMIASIS.

LESTER, H. M. O. **Further Progress in the Control of Sleeping Sickness in Nigeria.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, July, v. 38, No. 6, 425–44. [10 refs.]

In this paper the author continues his account of sleeping sickness control work in Nigeria, to which he referred in 1939 [this *Bulletin*, 1940, v. 37, 7]. He introduces his statement by a description of the characteristics of the disease as it is seen in Nigeria. Three forms are distinguished, the mild form (which is the most common and in which death is often due to intercurrent disease after a long period of ill-health), the toxic form (which is much more rare, and in which death may rapidly supervene) and the nervous form (with

the characteristic sleeping sickness syndrome). Human trypanosomiasis became widespread when, as a result of suppression of tribal wars, people left the walled villages with their intensive surrounding agriculture and scattered into closer contact with the flies. There is now a correlation between the areas of infection and the lines of communication.

At first an attempt was made at control by a voluntary system of treatment, but experience soon showed this to be insufficient, and compulsory surveys, with mass treatment, were therefore started. The system is not carried to the same lengths as in the Belgian Congo, where the aim is to examine every person twice each year for all the common diseases. This entails a very large staff and at one time there were 180 medical officers, 280 *agents sanitaires* and subordinate staff engaged on the work ; each person was provided with a passport on which details of medical examination were recorded. In Nigeria, however, social conditions and the mildness of the disease were taken into account, and the scheme adopted was less detailed than this ; it consisted of the provision of teams for initial surveys and mass treatment, and of permanent treatment centres, at which attendance is voluntary after the main treatment has been completed. From these centres small surveys can be carried out, and there is reason to believe that any recrudescence of the disease would soon be detected from the records of attendances and treatment. If incidence is reduced to about 1 per cent. of the population, these centres are adequate for control. provided that new outbreaks are quickly dealt with.

The standard treatment now consists of three 1-gramme doses of antrypol followed by five 2-gramme doses of tryparsamide, at intervals of five days, but the author gives an emphatic warning that a preliminary dose of 0·2 gm. antrypol should be given because, with a larger initial dose, alarming collapse, or death, may occur about once in 2,000 cases. In relapses such as are treated at the permanent dispensaries the standard course of tryparsamide is 17 grammes, or even more, after the three injections of antrypol. There is no evidence that tryparsamide-resistant strains of trypanosomes have been produced as a result of mass treatment in Nigeria, but such strains have been produced where treatment is haphazard under a voluntary system. There is, however, no evidence of the spread of resistant strains by tsetse, under natural conditions.

In a table which summarizes the work done from 1931 to 1943, it is shown that the peak of infection was reached in 1935, when the rate was 20·5 per cent. in the populations surveyed, and that this has been reduced to 1·3 per cent. in 1942, and 2·1 per cent. in 1943. The great mass treatment effort was exerting its effect in 1936–40. In all, over three million people have been examined in new surveys, and over 900,000 in re-surveys, during the period.

The sleeping sickness dispensaries have developed, to include general medical and health work, and provision has been made for the staff to be trained on those lines, so that the dispensaries should become rural health centres ; by the end of 1943 there were 43 dispensaries, with 9 others under construction. Dispensary attendants trained in sleeping sickness work were also posted to 29 of the ordinary native administration dispensaries.

Tin mining has been a source of trouble. The miners suffered severely because their work was alluvial mining along the beds of streams heavily infested with tsetse. To control this it has been made compulsory for all miners to be medically examined every six weeks. This has been effective, and the treatment given has reduced the rates of infectivity, not only in the miners themselves, but also in the neighbouring villages. In the gold fields also the examination and treatment of miners has effected a dramatic reduction ; the rate has fallen from 35 to 0·4 per cent. Lester discusses the possibility of prophylactic injection of antrypol, but argues against it because of the danger of collapse after the injection, a danger to which it would be unjust to expose healthy men.

The tsetse flies concerned with sleeping sickness in Nigeria are *Glossina palpalis*, *G. tachinoides* and *G. submorsitans*. Clearing work has been done in the last few years to drive back the fly from immediate contact with human habitations and watering places, and to protect the fords and traffic routes. For the river-haunting flies the amount of clearing needed has been too small to cause serious deforestation, and the methods used, developed largely from the work of NASH, have been successful, so that in two provinces about 240,000 people are now protected. The Nigerian policy with regard to game destruction is one of *laissez-faire*, because to reduce game would be to drive *G. palpalis* and *G. tachinoides* to depend upon man and domestic stock, and to increase game would be to increase *G. submorsitans*.

Sleeping sickness settlements are not easily created in a country so closely inhabited as Nigeria, and fly-free areas are rare in that well-watered land. But where the infection rates are high, the concentration of the population in cleared country is deemed justifiable, as in the eastern part of the Zaria province, where the rate was as much as 50 per cent. After much detailed preliminary work, which has been described in this *Bulletin*, the great Anchau corridor was prepared, and at present includes 480 square miles of fly-free country, in which model compounds have been constructed, and where special attention had been paid to hygiene and to agriculture and stock raising.

The result of these activities has been that sleeping sickness is now almost under control. The depopulation which was taking place when the disease was at its height has been reversed to an increase in population, but the fact that 21,000 cases were treated in 1943 shows that constant vigilance is necessary. [The author, and those who have been associated in this work, must be congratulated in these results, largely achieved in war time when staffs have been greatly reduced.] Research has lately been suspended, but proposals have already been made for a Central Trypanosomiasis Research Institute, to be established in Northern Nigeria, and to serve the whole of British West Africa. *Charles Wilcocks.*

NIGERIA: REPORT ON THE MEDICAL SERVICES FOR YEAR 1943. Appendix B pp. 19–21. **Sleeping Sickness Service.**

In 1943 the number of cases of sleeping sickness treated was about 21,300, of which 19,000 were dealt with by the Sleeping Sickness Service (5,321 at mass surveys, 13,100 at dispensaries and 540 at the mines); 830 were treated at missions and 1,500 at general medical stations. There was no evidence of any general increase of the disease, though the total cases treated were greater than in the previous year, partly because more permanent dispensaries had been established. Surveys and spot re-surveys were carried out, and incidence rates of 3·8, 2·6, 1·0, 1·3, 0·2, 0·5 and 2·1 per cent. were found.

Permanent treatment centres are established where surveys have been completed; there are now 43 of these, and 29 Native administration dispensaries. At these, in addition to the 13,100 cases of sleeping sickness, 75,000 general cases were dealt with. In the mining areas the whole labour force of 6,000 was examined every six weeks, and it was found that an average of 1·4 per cent. of the labourers contracted sleeping sickness every six weeks. But for these examinations and treatments, rates of 20–40 per cent. would have again been general on these mines [where the work is alluvial, with intense exposure to tsetse].

Work on the Anchau settlement is continued; the system of partial clearing and barrier clearing used in much of the corridor is completely effective. Improvements in agriculture and stock farming are being continued.

In a conference with representatives from French and Belgian territories, arrangements for closer co-ordination were made, and a proposal was framed for the establishment of a Central Trypanosomiasis Research Institute.

Charles Wilcocks.

RODHAIN, J. & VAN HOOF, M. T. Au sujet d'un élevage de " Glossina palpalis " en Europe et de quelques essais d'évolution chez cette glossine des " Trypanosoma lewisi " et " cruzi." [**The Rearing of** *G. palpalis* **in Europe : Attempts to infect it with** *T. lewisi* **and** *T. cruzi*.] *Ann. Soc. Belge de Méd. Trop.* 1944, June 30, v. 24, Nos. 1–2, 54–7.

VAN GOIDSENHOVEN, C. & SCHOENAERS, F. Sur la stabilisation des antigènes utilisés au sérodiagnostic des trypanosomiases. [**The Stabilization of Antigens used in the Diagnosis of Trypanosomiasis.**] *Ann. Soc. Belge de Méd. Trop.* 1944, Sept. 30, v. 24, No. 3, 167–73.

Complement fixation tests were made with antigens prepared in various ways with *Trypanosoma equiperdum* obtained by fractional centrifugation of heavily infected blood. The chief defect was instability ; antigenic activity became progressively less with keeping and anticomplementary power became progressively greater. Various antigens tried, *e.g.*, ZOTTNER's [this *Bulletin*, 1934, v. 31, 593], MARKOWIECZ's alcoholic antigen (*Deut. Tierärzt. Woch.*, 1941, v. 49, 578), and LUGOMER's antigens (*Jugo-slav. Vet. Glasnik.*, 1940, v. 20, 300) were found unsatisfactory, and the authors could not confirm WATSON's view that frozen antigen would keep indefinitely.

A satisfactory antigen was finally prepared with the co-operation of RESSELER (see *Ann. Soc. Belge Méd. Trop.*, 1944, v. 24, 29). The centrifuged deposit of trypanosomes was frozen, distributed into ampoules, and dried in a vacuum at about —75°C. for an hour, after which the ampoules were sealed *in vacuo*. This preparation was found to have preserved its antigenic power and a low anticomplementary activity for 16 months ; further tests may enable the time limit of preservation to be determined.

J. F. Corson.

FIENNES, R. N. T. W., JONES, E. R. & LAWS, S. G. **The Course and Pathology of** *Trypanosoma congolense* **(Broden) Disease of Cattle.** 13 typed MS. pp., 22 figs. [59 refs.] 1945. Veterinary Research Laboratory, Entebbe, Uganda.

Native cattle, adults and calves, in Uganda were experimentally infected by subcutaneous injection of local virulent strains of *Trypanosoma congolense*, and the resulting disease was studied by clinical observations, morphological and chemical examination of the blood and histological examination of the tissues.

The blood showed a great diminution in the number of erythrocytes and a corresponding decrease in haemoglobin ; the chemical determinations were almost always within the physiological range.

Although histological examination of the tissues supported the view that *T. congolense* is essentially a blood parasite with no invasion of the tissues, severe pathological changes in the tissues were produced ; there was a widespread round-celled infiltration leading to fibrosis and necrosis. The organs most severely affected were the kidneys, adrenals, pancreas, thyroid and pituitary. The authors regard these changes as primary and the anaemia as secondary. The fever was of a relapsing type ; in adult cattle the disease was usually fatal but calves usually recovered, with immunity to homologous

strains but not to heterologous strains of the parasite. [No microscopic examinations appear to have been made of the cerebrospinal fluid, or of the pericardial, pleural, and peritoneal fluids.] *J. F. Corson.*

MAZZA, S., MIYARA, S. & JÖRG, M. E. Investigaciones sobre enfermedad de Chagas. Exámenes histológicos de biopsias de conjuntivas en primer periodo de enfermedad de Chagas. [**Histopathology of the Conjunctiva in the Early Stage of Chagas's Disease.**] *Universidad Buenos Aires: Mision de Estudios de Patologia Regional Argentina (Jujuy).* Publicación No. 68. 1944, 80 pp., 76 figs. & 2 charts.

The authors have had the opportunity—and have taken full advantage of it—of examining sections of the conjunctiva taken by biopsy in the first stage of this disease.

They are careful to distinguish acute primary conjunctivitis from the secondary inflammatory reaction set up by extension from without. Only 4 per cent. of cases presented the former. It is characterized by conjunctival erosion, much polymorphonuclear infiltration, distributed close to the epithelium, with leishmania in numbers beneath the necrotic eroding zone. This leucocytic infiltration is very dense, but does not invade the depth of the corium of the mucosa. Lymphatics are inflamed and appear as bands spreading to the submucosal vessels.

In the secondary inflammation the epithelium is affected, with eroded patches and hyperplastic and atrophic changes mingled. The subepithelial inflammatory tissue is composed in great part of plasmocytes, with, in some cases, a moderate proportion of lymphocytes. In more than half the cases there is massive histiocytic proliferation, with giant cells in the interior of the infiltrated focus, and leishmania in about one-fifth of the cases.

Eight cases of the primary form are presented, with much clinical detail: a history of the patient's illness, the clinical state, the condition of the heart, the course of the disease and the treatment adopted.

As regards the eye lesions and their histopathology, with which the monograph is concerned, there is such a wealth of detail that we can give only a summary here; there is swelling and oedema of the corium with extensive congestion of the capillary vessels, dilatation of the lymphatics and small haemorrhages; infiltration in the deeper part of the corium, spreading gradually towards the epithelial layers and this may extend as a covering below the basal layer as a thin lining, which the authors designate subepithelial permucous lymphangitis. The infiltration finally assumes the form of either a subepithelial stratum or a fusion into subepithelial nodules or granulations. Below the infiltration is oedema with sparse leucocytic invasion, while above the granulations (or nodules) or denser infiltration, erosion and ulceration take place with marked leucocytic invasion.

Photographs of the patients show the general condition, while a series of photomicrographs illustrate the histological changes. *H. Harold Scott.*

FEVERS OF THE TYPHUS GROUP.

DONOVICK, R. & WYCKOFF, R. W. G. **Tests of Epidemic Typhus Vaccines.** *Pub. Health Rep.* Wash. 1945, May 18, v. 60, No. 20, 560–63.

This paper was approved for publication on September 11, 1942, but because of the subject it has not been published till now.

The authors have produced evidence to show that great improvements had been made during the preceding year in the efficacy of the typhus vaccines, and also that the titres of the complement-fixation reaction in the sera of vaccinated guineapigs is a reliable indication of the potency of the vaccines. The results of the experiments on which these claims are based are shown in a table, from which the reviewer has compiled the abbreviated table shown below. In the original table full details are given of the febrile reaction of each guineapig after a challenge intraperitoneal injection of brain substance of guineapigs infected by the Breinl strain of rickettsiae ; the table below contains, instead, a statement of the average number of days on which the animals showed a febrile response of 39·7°C. or over ; these temperatures have been taken by the authors as indications of a significant febrile reaction. The number of days on which the temperatures were recorded was 10, starting from the 6th day after the administration of the challenge injection. The complement-fixation tests were carried out three days after the second, and ten days after the first dose of vaccine had been given.

All the three types of vaccine were prepared from a "common pool of inactivated yolk membrane" ; vaccine I A was made by a development of the original Cox method ; vaccine II A was similar except that phenol was replaced by "another chemical" ; vaccine III A was processed on lines suggested by N. H. Topping.

Vaccine dose (cc.)	Vaccine	Average febrile days after challenge	Average comp. fixn. titre	Number of guineapigs tested
0·1	I A	5·33	1–2	3
0·1	II A	2·00	1–16	3
0·1	III A	0	1–64	2
0·25	I A	3·5	1–32	2
0·25	II A	1·33	1–32	3
0·25	III A	0	1–128	2

In control, unvaccinated guineapigs challenged in the same way, the average number of febrile days was seven.

It is stated that vaccines made a year or more before the date of these experiments would probably not have given a demonstrable degree of protection or have been followed by a complement-fixation titre in excess of 1–2 when administered in comparable conditions. *John W. D. Megaw.*

Fitzpatrick, Florence K. **Vaccination of Mice against Typhus.** *Proc. Soc. Exper. Biol. & Med.* 1945, Mar., v. 58, No. 3, 188–90.

Yolk-sac vaccines were injected intraperitoneally into mice which were tested for immunity 7 days later by intravenous or intraperitoneal injections of infected yolk-sac material.

Of 54 mice immunized by various doses of epidemic-typhus vaccine, 53 survived 24 hours after receiving intravenous injections of epidemic-typhus rickettsiae which killed 49 out of 54 unvaccinated mice within the same period. A dose of as little as 0·1 cc. of a 10 per cent. yolk-sac vaccine protected all but one of 8 mice.

All of 16 mice protected by the same epidemic vaccine survived 24 hours after being inoculated with a dose of murine rickettsiae which killed 3 of 16 unprotected mice ; in this case 8 of the 16 vaccinated mice died within 7 days

as compared with 12 of the 16 control mice, and it should be noted that the live murine rickettsiae were injected into the peritoneum, not into the vein as in the previous series.

All of 8 mice protected by murine vaccine were found immune to intravenous injections of live murine rickettsiae, whereas all of 8 control mice died within 24 hours when challenged in the same way; all of 8 mice similarly protected by murine vaccine were found immune to intraperitoneal injections of live murine rickettsiae, while 5 of 8 controls died within 24 hours and the remaining 3 died after 7 days.

Of 8 mice protected by 0·5 cc. of a 10 per cent. yolk-sac suspension of killed murine vaccine 3 survived 24 hours after being challenged by doses of epidemic rickettsiae which killed all of 8 control mice in the same period.

The use of mice has two advantages; it eliminates the need for guineapigs and enables the period of testing to be shortened by about two weeks.

The results are said to suggest that the toxic factor in epidemic and murine strains of rickettsiae is identical. *John W. D. Megaw.*

CLAVERO, G. & PÉREZ GALLARDO, F. Estudios sobre la cepa E de rickettsia Prowazeki viva en la inmunización humana. [**Studies of Live "Strain E" of *Rickettsia prowazeki* in the Immunization of Human Beings.**] *Rev. Sanidad e Hig. Pública.* 1944, Nov., v. 18, No. 8, 547–60.

The authors describe the results of further investigations into the "non-pathogenic and immunizing strain of *R. prowazeki*" whose discovery they announced in June 1943 [this *Bulletin*, 1944, v. 41, 24].

After preliminary tests with fresh living cultures, the authors have now prepared a vaccine by desiccation in the manner employed in the preparation of yellow fever vaccine, and have inoculated 2,217 persons in various parts of Spain where there was some risk of infection. Although no case of typhus fever has occurred among any of the vaccinated persons, the authors do not claim that the efficacy of the vaccine has been established, but they have found that the Weil-Felix reaction becomes positive at titres of 1–40 to 1–640 in nearly half of the persons tested after inoculation. The strength of the reaction was not found to be affected by the dose of the live vaccine that was administered. Only one person had a reaction which might have been regarded as a mild attack of typhus fever; in this case there was continued fever from the 10th to the 21st day after inoculation.

The local and general reactions that occurred in a few cases were not more severe than those following T.A.B. inoculation. *John W. D. Megaw.*

HOARE, E. D. **Some Additional Observations on the Presence of Agglutinins to *Proteus OX19* in the Serum of Pregnant Women.** *Monthly Bull. Ministry of Health & Emergency Pub. Health Lab. Service (directed by Med. Res. Council).* 1945, June, v. 4, 125–8.

Like NELSON and CRUICKSHANK [this *Bulletin*, 1945, v. 42, 363] the author has been unable to confirm the claim made by GRATCH that the sera of pregnant women agglutinate *Proteus OX19* at high titres [this *Bulletin*, 1944, v. 41, 197]. Using suspensions issued by the Oxford Standards Laboratory, he found that only one of 28 such sera reacted at a titre of 1–125. The readings were made after 3-hours' incubation at 37°C. and 18 hours in the ice chest.

He then used a living culture of *Pr. OX19*, selected from four strains as being the most sensitive, and carried out slide-agglutination and the usual tube-agglutination tests, with the results shown in the table. In the slide test a portion of a colony was suspended in a drop of serum, either undiluted or diluted as shown in the table:—

	Slide Test					Tube Test				
	Positive at dilution of					Positive at dilution of				
	Sera tested	Undil.	1–2	1–4	1–8	Sera tested	1–25	1–50	1–125	1–250
Control	13	2	4	7	0	13	2	7	4	0
Pregnant ...	61	4	18	24	15	41	5	17	18•	1

Although the average titre of agglutination was higher in the sera of pregnant than of non-pregnant women the difference was not enough to form the basis of a test for pregnancy.

Sohier, R., Parnet, J. & Chon, A. Recherches sur les réactions consécutives à l'injection intradermique de suspensions formolées de Rickettsies chez l'homme. [**Reactions following Intradermal Injection of Formolized Suspensions of Rickettsiae in Man.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 1–2, 15–18.

Wu, C. C. & Chi, C. Y. **Typhus Fever—a Clinical Study of 94 Cases.** *Chinese Med. J.* (Chengtu Edition). 1944, Jan., v. 62A, No. 2, 67–70. Also in *Chinese Med. J.* Washington. 1944, July–Sept., v. 62, No. 3, 221–6.

Between October 1938 and November 1940, 94 cases of typhus fever, believed to be louse-borne, were seen by the authors at the Central Hospital, Kweiyang, Hunan Province, South China. The evidence pointed strongly to case-to-case infection. Among the 18 members of the staff who were attacked all but two had been in close contact with hospital patients; no case of the disease occurred in July or August 1939, the peak periods being November or December. In some cases attempts were made to isolate rickettsiae, but without success.

All the patients recovered, and it is stated that in 1937, Hsieh *et al.* [this *Bulletin*, 1938, v. 35, 362] reported 14 cases from Changsha and suggested that the mildness of the disease pointed to the occurrence of a strain of infection less virulent than that of North China. [It would not be surprising if the disease occurred in a mild form in South China where the climatic conditions are relatively unfavourable to louse transmission.]

The clinical features were of the type usual in mild forms of typhus fever; the onset was sudden in 58 cases and gradual in 36; the usual duration of the fever was 12–16 days, and the fall of the temperature was by lysis in 84 cases. The Weil-Felix reaction became positive before the end of the first week in four of the 68 cases in which the test was carried out; in 22 it first became positive after the 14th day. The total leucocyte count was less than 5,000 per cmm. in 11 cases, and more than 10,000 in 21. There was bronchitis in 17 cases and cough in 53. The maculopapular spots were scanty in 40 cases; they became petechial in 41, in most of which the rash was profuse and the symptoms rather severe. No mention is made of the occurrence of septic or thrombotic complications. *John W. D. Megaw.*

Laskin. [**Epidemiological and Diagnostic Value of the Investigation of Lice for Rickettsia.**] *Sovetskaia Meditsina.* Moscow. 1944, No. 12, 15–17. [In Russian.]

Films were made from the gut of lice collected from supposed cases of typhus and were stained with Giemsa. In positive cases rickettsiae were found in large

numbers in the gut cells ; they could be easily distinguished from non-pathogenic forms, which were larger and extracellular. Rickettsiae were present in gut smears of 8 of 15 lice collected from a case of typhus ; 12 lice were collected from a second case, and rickettsiae were found in nine. The test was also positive with lice from four members of the medical staff exposed to risk of infection ; three of these developed typhus after 9 to 13 days. In the fourth subject, who remained well, lice were present in the outer clothing only. The test is useful in the early diagnosis of typhus, since lice on the patient become infected in the first few days of the illness, whereas the Weil-Felix reaction does not become positive until the seventh or eighth day. *D. J. Bauer.*

HAMILTON, H. L., PLOTZ, H. & SMADEL, J. E. **Effect of p-Aminobenzoic Acid on the Growth of Typhus Rickettsiae in the Yolk Sac of the Infected Chick Embryo.** *Proc. Soc. Exper. Biol. & Med.* 1945, Mar., v. 58, No. 3, 255–62, 5 figs.

This report was presented to the U.S.A. Typhus Commission in December 1943, but was withheld from publication at that time.

Previous experiments by SNYDER, MAIER and ANDERSON (*Rep. to Div. Med. Sci.*, Nat. Research Council, Washington, 1942, Dec. 26) and by ANDREWES, KING, VAN DEN ENDE & WALKER [this *Bulletin*, 1945, v. 42, 20] had suggested that para-aminobenzoic acid ("PABA") inhibited the growth of rickettsiae in infected animals.

The authors describe tests of the action of the drug on the organisms growing in yolk sacs. The survival time of the chick embryos was prolonged and the number of rickettsiae in yolk-sac smears was greatly reduced by suitable doses of the drug injected into the yolk sacs on the day before inoculation with rickettsiae ; and a surprising degree of inhibition of the organisms was caused by injections given up to two days after inoculation of the yolk sacs.

The maximum inhibition was caused by relatively massive doses of 2–4 mgm. for each egg, but it was also found that large doses of 4 mgm. caused delayed death in a significant proportion of uninfected embryos.

The results were the same with both epidemic and murine rickettsiae.

John W. D. Megaw.

BILIBIN. [**Typhus in Vaccinated Subjects.**] *Sovetskaia Meditsina.* Moscow. 1944, No. 12, 14–15. [In Russian.]

Forty cases of typhus occurring in vaccinated persons were studied ; 30 of these were experimental infections in volunteers. The febrile period was short (less than eight days in 30 per cent. and less than 10 days in 50 per cent. of cases). The onset was rapid with rise of temperature without prodromal symptoms ; marked fluctuations between morning and evening readings were common (1°C. in 20 cases, 2°C. in 14 cases). The exanthem was scanty and roseolar, but was entirely absent from 13 cases ; a typhoid state was seen in two cases only. Complications were rare (occasional bronchitis) and convalescence was rapid. The titre of the Weil-Felix reaction was never high (1/40–1/160), becoming positive at the end of the febrile period. This, together with the mild and atypical nature of the disease, renders the diagnosis of typhus difficult in vaccinated subjects. *D. J. Bauer.*

VARGAS, R. Aislamiento de una cepa de tifo murino en El Salvador. [**Isolation of a Strain of Murine Typhus in Salvador.**] *Bol. Oficina Sanitaria Panamericana.* 1944, Nov., v. 23, No. 11, 980–83. English summary.

In June 1943 a consistently orchitic strain of rickettsia was isolated from a patient on the 9th day of an attack of typhus fever ; the patient's serum

reacted at a titre of 1–256 with the complement-fixation test when a murine antigen was used ; with an epidemic antigen the reaction was negative. The test was carried out at the Army Medical Centre, Washington.

The strain was maintained through 14 consecutive passages in guineapigs.

The fleas of more than 400 rats caught in San Salvador were tested by inoculation into 256 guineapigs, with negative results, but in a footnote the author states that in December 1943, rickettsiae were isolated from the fleas of rats caught in one quarter of San Salvador.

The clinical features of the disease in the patient were very similar to those seen in other typhus cases in Salvador. *John W. D. Megaw.*

MEGAW, J. W. D. **Scrub Typhus as a War Disease.** *Brit. Med. J.* 1945, July 28, 109–12.

Seldom has a disease emerged from comparative obscurity to notoriety so rapidly as has scrub typhus. Its limitation to " typhus islands " in primary and secondary jungle, inherent in its rickettsia-mite-rodent cycle, placed only sparse rural populations at risk until recently. It rarely obtruded in medical statistics, and claimed the attention of only a few investigators in Malaysia and adjacent territories, who were attracted largely by its kinship to the fevers of the typhus group. Since 1942, however, the ebb-and-flow of jungle warfare in those regions has vastly increased the populations at risk ; man in unprecedented numbers has, in some degree, supplanted the rodent as a host of the infected larval mite, and the incidence of the disease has correspondingly soared. An average mortality of 10–15 per cent., a high incapacitation rate, and a depressing psychological effect has compelled intensive investigation by clinician, entomologist and virus worker in South-East Asia and in the South-West Pacific. New minds and new methods have already greatly supplemented our previous knowledge of scrub typhus, and devised effective counter-measures. The incorporation of these (as far as security considerations permit) into this succinct report by so able a pioneer and so lucid an exponent in this field as Sir John Megaw is therefore most timely and valuable.

In discussing classification, the author stresses the advantage of viewing scrub typhus in its true perspective as one of the four comprehensive groups of typhus-like fevers, louse-borne, flea-borne, tick-borne and mite-borne. To the clinician especially this is advantageous. Apart from the occasional occurrences of a necrotic ulcer at the site of the inoculation of the virus in scrub typhus and in the tick-borne *fièvre boutonneuse*, the clinical syndromes, including even such rare complications as parotitis and venous thrombosis, are remarkably similar in all of the four groups. To the epidemiologist the association of the louse, flea, tick and mite in the nomenclature contrasts the genesis of the human or " demic " louse-borne typhus with that of the " zootic " members of the group. [It may be added that to the pathologist and the virus worker the similarities shared by the four groups are less fundamental. The human morbid anatomy and morbid histology are similar ; the causal organism is a *Rickettsia*. But the experimental pathology, in its widest interpretation, of mite-typhus is in so many aspects so different from that of the other three members of the typhus group of fevers that the virus worker of post-war years will probably prefer to retain such individual names as *fièvre boutonneuse*, Rocky Mountain spotted fever, epidemic louse-borne typhus, endemic flea-borne typhus, tsutsugamushi, to mark differences that refinements of laboratory technique can demonstrate.

Referring to certain special features of scrub typhus, the author notes that the disease is not new, having, as tsutsugamushi, been known in Japan for

many years, and in China probably for centuries. The presence of the necrotic ulcer is not a *sine qua non* in the differential diagnosis. A disease of scrub-land in South-East Asia and the South-West Pacific, it has literally dogged the footsteps of the Allied armies operating in those areas.

It is pleasing to see the name *R. tsutsugamushi* preferred to that of *R. orientalis* for the causal organism. For the organism was demonstrated in the testis of infected rabbits and the former name given to it by OGATA two years before NAGAYO *et al.*, working with the "Chiba" strain obtained from Ogata and with three strains from other sources, re-demonstrated the organism in material from the eyes of rabbits, and in a report that received much greater publicity outside Japan than did Ogata's earlier report, quite unjustifiably renamed the organism *R. orientalis*.

The salient known facts concerning the mite and its habitat are given, and indicate clearly the many problems that confront the epidemiologist in attempting to cope with the disease by prediction and counter-measure. [The convenient term, "blood-meal" of the mite, should probably give way to the term "tissue-meal" or "lymph-meal"; for it is now believed, on secure histological observation, that the larval mite, after attaching, obtains its nourishment by pre-digesting by salivary secretion the tissues of its host at the point of attachment, to form a "histosiphon."]

In its pathology scrub typhus is a disease of the smaller blood-vessels; the vascular endothelial cells are invaded; there is perivascular infiltration. Only exceptionally does convalescence fail to bring complete recovery from these lesions and their effects.

The clinical features are described in considerable detail; and certain features are stressed which have puzzled many clinicians new to the disease, such as the undoubted occurrence of outbreaks of greatly differing degrees of virulence, the inconstancy of leucopenia as a diagnostic point, and the differing incidence of the ulcer in light and dark-skinned patients.

The Weil-Felix test yields positive agglutination of the *OXK* strain of *Proteus*, and continues to be of great value, provided that the strain of *Proteus* used is not maltreated and that interpretation is made with due regard to standards evolved by earlier serologists in this field. [Many observers would place the attainment of maximum titre in the fourth rather than in the second week after onset.]

Diagnosis affords little difficulty to the clinician experienced in the disease, although, unless the eschar be present, he will usually desire to see the patient more than once in the first week before giving a confident diagnosis. Dengue, flea-borne and tick-borne typhus need to be excluded; louse-borne typhus less so in the present combat areas. [Leptospirosis might well be added.]

In treatment, chemotherapy and serum-therapy have as yet failed. The minimum of transportation and the most expert nursing are two cardinal considerations. An adequate intake of fluid should be ensured. Supportive intravenous treatment should be undertaken only when expert laboratory help is available. [In this connexion, recent observations made in Australia indicate the occurrence of marked diuresis a day or two before defervescence, and, by implication, the possible promotion of pulmonary oedema by excessive intravenous fluids. Additional data on this point from different areas would be most valuable.]

Concerning prevention, methods of mite-avoidance, based on our knowledge of the mite and its host, are enumerated. But, for security reasons, mention of certain other effective methods of prophylaxis, the result of recent investigations, are withheld. *R. Lewthwaite.*

J. Amer. Med. Ass. 1945, June 16, v. 128, No. 7, 519. **Protection against Scrub Typhus Mite.**

" The War Department recently announced that the Office of the Quartermaster General, on recommendation of the Office of the Surgeon General, is replacing dimethyl phthalate with benzyl benzoate for use in clothing impregnation for protection of troops against the scrub typhus mite, so prevalent in the South Pacific. Clothing impregnated with benzyl benzoate will withstand more launderings before treatment is necessary than those impregnated with dimethyl phthalate. Clothing is dipped in an emulsion of 5 per cent. benzyl benzoate in water. One treatment is effective for about two weeks."

Patiño-Camargo, L., de Zulueta, J. & Toro, G. Persistencia del virus de la fiebre petequial de Tobia en el Argasidio *Ornithodoros parkeri*. [**Persistence of the Virus of the Spotted Fever of Tobia in** *Ornithodorus parkeri*.] *Bol. Oficina Sanitaria Panamericana.* 1944, Nov. v. 23, No. 11, 978–80. [10 refs.] English summary (5 lines).

An adult tick, *O. parkeri*, which had fed, on October 29, 1940, on a guineapig infected with the spotted fever of Tobia, was titrated and injected into guineapigs 1,087 days afterwards. The infection was found to be almost as intense as that produced by the same rickettsial strain when the tick was originally infected. The strain was passed through 13 successive guineapigs. About three-fourths of the inoculated guineapigs died, and there was a scrotal reaction in 47 per cent. of the male guineapigs used in making the passages.

A related species of tick, *Ornithodorus rudis*, is abundant in Tobia ; it has been shown to be a potential vector of the local spotted fever, and so may be important in maintaining and disseminating the disease.

John W. D. Megaw.

Blair, R. K. & Bader, M. N. **Observations on Experimental Bullis Fever in Man.** *Texas Reports on Biol. & Med.* 1945, v. 3, No. 1, 105–11.

Nine healthy young men were inoculated subcutaneously with spleen substance obtained from guineapigs infected with " rickettsia strains " regarded as the cause of Bullis fever.

Five of the volunteers received a strain of the 16th guineapig passage originally isolated from a tick, *Amblyomma americanum*, collected in the Fort Bullis area ; the other four were inoculated with a strain isolated from a patient suffering from the disease ; this strain was regarded as identical with the tick strain. [Many other attempts to isolate the causal organism from patients by cultural and animal-inoculation methods had failed.] The febrile responses in the volunteers were as variable as those already observed by the authors in guineapigs. With the tick strain they were :—(1) fever (99–99·2°F.) daily for four days, (2) no fever, (3) low-grade fever for 19 days, (4) low-grade fever for 16 days, and (5) low-grade fever for 24 days. With the human strain two of the patients had no fever, one had a daily rise to 99–99·4°F. for five days, and another had low-grade fever for 28 days.

In seven of the nine patients there was leucopenia with a relative lymphocytosis, the lowest total counts being 3,700–4,900 per cmm.

[See this *Bulletin*, 1945, v. 42, 639] for a previous reference to the specificity of the Bullis fever rickettsia.] *John W. D. Megaw.*

Brennan, J. M. **Field Investigations Pertinent to Bullis Fever. Preliminary Report on the Species of Ticks and Vertebrates occurring at Camp Bullis, Texas.** *Texas Reports on Biol. & Med.* 1945, v. 3, No. 1, 112–21.

The author states that Bullis fever is the name given to an apparently new disease, presumed to be rickettsial, endemic at Fort Bullis, and strongly

suspected of being transmitted by a tick, *Amblyomma americanum*, though a mite, *Eutrombicula alfreddugesi*, may possibly be concerned.

The area, of about 30,500 acres, is semi-arid and uncultivated ; the vegetation consists of grass, junipers, oaks, thorny shrubs, and tangles of vines. Ticks of 12 species were found ; the most abundant was *A. americanum* which feeds on numerous hosts, including man, and is known to be a vector of Rocky Mountain spotted fever. *Haemaphysalis leporis-palustris* was fairly abundant on rabbits in the area ; it transmits Rocky Mountain spotted fever and tularaemia among animals but is not known to bite man. [STEINHAUS and PARKER (this *Bulletin*, 1945, v. 42, 375) have isolated a filter-passing virus from two lots of this tick caught on rabbits in the Fort Bullis area.] The most abundant of the 22 mammals found in the area were : the white-tailed deer (*Odocoileus virginianus*), the jack rabbit (*Lepus californicus merriami*), the armadillo (*Dasypus novemcinctum texanum*) and the grey fox (*Orocyon cinereoargenteus* subsp.); the racoon (*Procyon lotor fuscipes*), the fox squirrel (*Sciurus niger limitis*) and the striped skunk (*Mephitis mephitis mesomelas*) were also common ; all the above harboured *A. americanum*. Small rodents were notably few in numbers and could not be important as hosts for the ticks.

Birds of 79 species were found ; the ground-inhabiting and bush-dwelling species were consistently infested by immature stages of *A. americanum*, and so were regarded as important in maintaining the tick population.

Snakes of 16, and lizards of 8, species were found ; more than half of these were infested by the chigger mite, *E. alfreddugesi*. *John W. D. Megaw.*

YELLOW FEVER.

LAGOS, NIGERIA. **Annual Report of the Yellow Fever Research Institute. 1944.** 39 typed pp., 1 fig. [10 refs.]

As a result of discussions between the Secretary of State for the Colonies, the Rockefeller Foundation and the West African governments, it was decided that work on yellow fever should be reopened, and the Yellow Fever Research Institute, practically closed since the departure of the Yellow Fever Commission in 1934, has therefore been re-established under Dr. J. C. BUGHER and Dr. R. G. HAHN of the Rockefeller Foundation. The Institute is situated at Yaba, Nigeria, and on its staff are an entomologist, a medical officer and a laboratory superintendent, all from the Colonial Medical Service, a zoologist has also been appointed. The Institute is financed and controlled as a joint venture by the cooperating authorities ; the Rockefeller Foundation members arrived towards the end of 1943.

The programme for 1944–45 includes investigation into the distribution of yellow fever, by means of a viscerotomy service, protection test surveys and study of suspected cases ; work on these lines has been going on. It is presumed that jungle yellow fever exists, but this has not been proved ; it will therefore be necessary to test animal susceptibility, to make protection test surveys in animals, and to undertake studies on possible vectors, of which only *Aëdes aegypti* is at present known. Finally, the question of the distribution and control of vaccine has received attention.

At Yaba a large mouse colony has been reorganized, and the system of breeding used in Bogotá (Colombia) has been set up. Details are given of this

and of the diet of the mice. The intracerebral protection test has been adopted as standard because it needs only 0·3 cc. serum, and for other reasons. The determination of the amount of virus in vaccine is a standard procedure.

" An ampoule is rehydrated in the amount of physiological saline solution customarily employed for vaccination. This is allowed to stand 20 minutes at room temperature and from this serial decimal dilutions are then made in 10 per cent. normal human serum in physiological saline. Twelve mice are inoculated intracerebrally from each dilution with each mouse receiving 0·03 cc. of the inoculum.

" The mice are observed for three weeks and the deaths recorded. The end-point of the titration is defined as that dilution of vaccine which will kill 50% of the mice under the conditions enumerated above. For example, if the calculated endpoint is at a dilution of 1 : 1,000, then it may be said that the original material contains 1,000 fifty percent mortality doses or, as has become customary, 1,000 m.l.d. in each 0·03 cc. In the 1 : 10 dilution used for vaccination, there will be 100 m.l.d. per 0·03 cc. or 1,700 m.l.d. in each 0·5 cc. dose as actually administered."

The authors point out that with a dose of 100 m.l.d. in man, there should only rarely be failure to immunize, but to make sure that a sufficient dose is injected, it has been considered advisable that not less than 1,000 m.l.d. shall be contained in each dose when the vaccine is shipped. These standards result in a minimum titre of 1 : 600 in vaccine distributed in West Africa ; batches with lower values are not approved for general distribution. Most batches have maintained their titre very well. During this period 13 blood specimens, taken after vaccination, have been tested for protection ; all except one were positive.

In August 1944, an outbreak of jaundice was reported from places on the Cross River. The most severely affected district was Unwana, where there were more than 1,000 cases, and 100 deaths. Yellow fever was suspected because the patients had fever, headache and albuminuria in addition to the jaundice. This outbreak was at once investigated, but although a number of cases were fatal, all the evidence pointed to the disease being infective hepatitis. Yellow fever and leptospirosis were excluded. The authors think that the very poor nutritional state of the people was distinctly a factor in the severity of the disease. The investigations, however, indicated that there had been a severe outbreak of yellow fever between 1930 and 1935, as a result of which almost one half of the population was infected. The authors point out that yellow fever in Africans rarely follows the usual textbook descriptions.

" The clinical concept of yellow fever must be a broad one and the physician should weigh the relative values of the presenting signs and symptoms. For example, severe jaundice associated with a relatively mild complex otherwise is sufficient to exclude the diagnosis of yellow fever. Further, albuminuria is the most constant finding in yellow fever and the failure to demonstrate it is a very strong argument against the diagnosis. In consequence it is concluded that the great majority of yellow fever cases in Nigeria are not recognised, especially in the African where the disease is so frequently mild."

In a pleasant and happy section of this report the story is told of the African Asibi, from whom was isolated, in 1927, the famous strain of yellow fever virus which bears his name and which was the origin of strain 17D, so widely used as a vaccine. Asibi was seen by Dr. MAHAFFY during his attack of yellow fever, and has now again been found by Mahaffy, his serum is still strongly protective. Arrangements have been made by which Asibi will receive a pension for life.

The final section of the report deals with tests made on certain sera which had been left behind at Yaba since 1931–33. Many of these had originally contained protective antibodies, and full details of the tests made at the time were discovered with them. They had been left in an outbuilding, exposed to all

the fluctuations of the surrounding temperature. In general there has been a marked reduction of protective power similar to that which occurs with diphtheria antitoxin under similar conditions ; the average loss was of the order of 50 per cent. per annum, but there were great variations in individual samples.

Charles Wilcocks.

Brazzaville [A. E. F.]: Rapport sur le Fonctionnement Technique de l'Institut Pasteur en 1943 [Ceccaldi, J., Director]. 49–56. Fièvre jaune. [**Yellow Fever.**]

Vaccination against yellow fever has been carried out during the year with three lots of vaccine (Nos. 138, 326, and 1074) received from the Rockefeller Foundation. A total of 719 persons were vaccinated, including 565 Europeans, 64 local subjects, and 90 natives. Four showed more or less severe reactions on the sixth day, which lasted for 48 to 72 hours. One lot of vaccine (No. 136), which had been kept for about 22 months in a Frigidaire at 8° to 10°C., when tested on mice was found to have lost its properties.

The " Dakar " neurotropic strain of yellow fever virus is recorded as being in its 456th passage in mice, and regularly kills animals in a dilution of 1/600,000. The Saleun-Ceccaldi strain, isolated at Dakar in 1937, is now in its 127th passage.

Serum protection tests were carried out in the village of Boundji (Likouala-Mossaka), on seven children ; one was positive and six negative. At Brazzaville the sera of five men were negative, but out of seven cattle two gave doubtful positives, and out of ten dogs two were definitely positive.

Yellow fever was diagnosed in two Italian prisoners of war who died at Fort Archambault (Tchad), by pathological examination. *E. Hindle.*

Lennette, E. H. & Perlowagora, Alina. **The Complement Fixation Test in the Diagnosis of Yellow Fever. Comparative Value of the Serologic and Histopathologic Methods of Diagnosis.** *Amer. J. Trop. Med.* 1945, Jan., v. 25, No. 1, 11–18. [22 refs.]

The authors have studied the relation between the clinical severity of yellow fever infection and the amount of complement-fixing antigen in the blood, and find that there is a correlation between them. This is in marked contrast to the amount of damage found in the liver at death, which seems to bear very little relation to the severity of the infection.

The microscopical lesions occurring in the liver in yellow fever cases are well known, but other conditions such as treatment with tannic acid may produce similar lesions (see Belt, *J. Path. & Bact.*, 1939, v. 48, 493). The authors inoculated 21 marmosets, *Callithrix jacchus*, and 2 monkeys, *Macaca mulatta*, with tannic acid. All these animals were examined for pathological changes in the liver and in 13 out of the 21 marmosets the histopathological features were indistinguishable from those considered characteristic of yellow fever. The changes included hyaline necrosis, fatty degeneration, and the development of typical intranuclear inclusions. The sera of these animals were examined for yellow fever virus and were uniformly negative.

A second table shows the results obtained in 10 marmosets and 4 *rhesus* monkeys, which died as a result of infection with yellow fever virus. The histopathological diagnosis was negative for yellow fever in 4 out of the 10 marmosets and 2 out of the 4 monkeys. Nevertheless, yellow fever complement-fixing antigen was present in the serum of every animal.

The results support the view that the complement fixation test constitutes a more accurate and reliable method of diagnosis of yellow fever infection than the histopathological examination of tissue such as liver. *E. Hindle.*

HARGETT, M. V. & BURRUSS, H. W. **The Use of Rhesus Monkeys in the Testing of Aqueous-Base Yellow Fever Vaccine.** *Amer. J. Trop. Med.* 1945, Jan., v. 25, No. 1, 19–30, 1 fig. [33 refs.]

The present method of yellow fever vaccination involves the use of living virus attenuated to such a degree that it no longer produces visceral infection in men or monkeys, yet the virus multiplies in the body and produces a high de ree of immunity. The authors, working in the Rocky Mountain Laboratory of the National Institute of Health, U.S.A., have tested 192 different lots of aqueous-base (serum-free) yellow fever vaccine in *rhesus* monkeys, and give the results of their experiments in a series of tables and charts.

Each monkey, *Macaca mulatta*, was inoculated intracerebrally with 0·25 cc. of yellow fever vaccine from a single homogeneous lot. Each inoculum contained 200 to 2,230,000 minimum lethal mouse units [LD_{50}]. The animals were observed for a minimum of 30 days after inoculation, and out of 200 monkeys none died of trauma or intercurrent disease.

Each monkey was bled on the 2nd, 3rd and 4th post-inoculation days to determine if virus was present in the circulation. Evidence of its presence was found in 192 animals (96 per cent.), more virus being present in those monkeys that had received a large dose of vaccine than in those receiving small doses.

Fever was shown by 167 monkeys, in the majority of cases on the 8th to the 10th days, and generally lasted for 2 days.

The sera of all the monkeys, except one, were examined both before and after vaccination by means of the mouse protection test. All the 199 animals were non-immune immediately prior to vaccination and all proved to be immune 12 to 33 days later. But of 102 animals receiving less than 200,000 m.l.d. of virus, 18 showed transient weakness with complete recovery, and 4 signs of severe encephalitis with extreme weakness with or without paralysis. Of these four, 2 were killed, 1 recovered and 1 had a residual paralysis of the right hind leg. Out of 98 animals receiving from 202,000 to 2,230,000 m.l.d. of virus, 24 showed transient weakness with complete recovery and 8 developed severe encephalitis. One of these died and the other 7 were killed. Histopathological study of the brains of the 10 monkeys examined post-mortem showed encephalitis in each case.

Twenty-two of the monkeys used had been previously infected with poliomyelitis, mumps, measles, or Rocky Mountain spotted fever, but no significant differences in their reactions were observed.

Of the 192 vaccines studied, 174 were released for human vaccination, mostly in the United States Army. No icterogenic or other untoward reactions have been recorded and it is evident that serum-free vaccine is preferable to that suspended in serum. *E. Hindle.*

DENGUE.

PITTALUGA, G. Sobre un brote de " Dengue " en la Habana. [**An Outbreak of Dengue in Havana.**] *Rev. Med. Trop. y Parasit.* Habana. 1945, Jan.–Feb.–Mar.–Apr., v. 11, Nos. 1 & 2, 1–3, 1 chart.

In October and November 1944 there was a sharp outbreak of dengue in certain quarters of Havana. The disease was well known in Cuba in the early years of the present century, but in recent times too little attention has been paid to it, perhaps because of the absence of epidemics and the difficulty of diagnosis of sporadic cases.

The clinical description is very brief; the fever is described as ending by crisis about the 4th day, and no mention is made of the occurrence of secondary rises of temperature. [Both of the charts with which the paper is illustrated are of the monophasic type, which often appears to predominate in places where the disease persists in endemic form. This monophasic type would be more likely to occur among patients who have a partial degree of immunity resulting from previous attacks.]

The rash appeared about the 5th day and lasted two or three days.

The author discusses the relationship of the disease to yellow fever, and states that although the viruses of the two diseases have been shown to be different, an experimental attack of dengue confers a partial degree of immunity on monkeys which are afterwards inoculated with the virus of yellow fever.

John W. D. Megaw.

Paul, W. D., Antes, E. H. & Sahs, A. L. **A Dengue-like Fever occurring in Iowa during the Poliomyelitis Epidemic of 1943.** *Arch. Intern. Med.* 1945, Mar., v. 75, No. 3, 184–91, 1 chart. [Numerous refs.]

The authors describe ten cases of a dengue-like fever in which a thorough physical, bacteriological, and serological investigation failed to disclose any causal agent. All but one of the patients were perfectly well within eight days of the onset. The occurrence was sporadic; there was no known contact between the patients, except that two brothers who had bathed in a creek about a fortnight before the onset were attacked on the same day. Three other patients had bathed in a lake, creek, or swimming-pool, a short time before the onset. There was no evidence of transmission by an insect. All the cases occurred in the late summer, six of them in August.

The fever was biphasic in three cases; the second phase was shorter and less severe than the first. In five patients there was slight generalized lymphadenopathy, and in one there was a fine maculo-papular rash on the extremities, but this might have been caused by sulphathiazole. There was leucopenia in three cases; the range of the leucocyte count was 3,750–15,000 per cmm.

Because of the general resemblance to dengue the authors prefer to call the disease a dengue-like fever; they call attention to the general resemblance between their cases and the diseases described under the following names:—(1) pretibial fever. (2) dengue-like fever (Cheney, in North California, 1934–35 [this *Bulletin*, 1936, v. 33, 446]). (3) Texas tick fever [Bullis fever]. (4) New disease entity (Bowdoin, in Georgia, 1940), and (5) Colorado tick fever.

The incidence of the chief features of these diseases is shown in a table in the article. In Colorado tick fever and Bullis fever the infection is regarded as being tick-borne; in pretibial fever, Bowdoin's fever, and the present series of cases, there is a suggestion that the infection may be water-borne.

John W. D. Megaw.

Lipscomb, Laura L. & McMahon, Jean L. **Pretibial Fever.** *J. Amer. Med. Ass.* 1945, May 12, v. 128, No. 2, 90–91, 1 fig.

A case is described which "clearly falls into the clinical category" of pretibial fever as described by Daniels and Grennan [see this *Bulletin*, 1944, v. 41, 278]. The fever lasted about nine days and was biphasic; the first phase lasted six days, the second less than two days. A rash resembling erythema nodosum appeared on the 5th day on the pretibial region, it faded somewhat at the end of the first phase but during the second phase it was "more brilliant than ever".

The spinal fluid, examined on the 3rd day contained 52 mgm. protein, and gave positive reactions with the Lange colloidal gold test and the Wassermann test (using cholesterinized antigen). *John W. D. Megaw.*

PLAGUE.

BROWN, J. H. **The Fleas (Siphonaptera) of Alberta, with a List of the known Vectors of Sylvatic Plague.** *Ann. Ent. Soc. Amer.* Columbus, Ohio. 1944, v. 37, No. 2, 207–13. [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, June, v. 33, Pt. 6, 88.]

A list is given of the 53 species of fleas known to be present in Alberta, where sylvatic plague occurs, showing their hosts and distribution there. Separate lists, based on the records of Eskey & Haas, are given of those among them that transmit plague and of the hosts on which these plague vectors have been found.

JELLISON, W. L. **Siphonaptera : the Genus *Oropsylla* in North America.** *J. Parasitology.* 1945, Apr., v. 31, No. 2, 83–97, 3 pls. [19 refs.]

" The American species of *Oropsylla*, namely *O. alaskensis*, *O. arctomys*, *O. idahoensis*, and *O. rupestris*, have been reviewed. Present records indicate the following host relationships and geographical distribution :

" *O. alaskensis* is restricted to the ground squirrels of the *Citellus parryii* group of the Far North, even entering the Arctic Circle.

" *O. arctomys* is a characteristic parasite of the woodchuck *Marmota monax*, but only very rarely occurs on other species of *Marmota* beyond the range of *M. monax*.

" *O. rupestris* appears to be limited to *C. richardsoni richardsoni*.

" *O. idahoensis* shows less host specificity and is found on a great many species of *Citellus* and also on *Cynomys* in the Western States, Canada and Alaska. It is the most characteristic flea parasite of the squirrel subgenus *Callospermophilus* and its range roughly coincides with this host except in the Far North.

" All species are found occasionally on rodents other than their normal hosts and frequently on predators within their range."

MUNTER, E. J. **Pneumonic Plague. Report of a Case with Recovery.** *J. Amer. Med. Ass.* 1945, May 26, v. 128, No. 4, 281–3, 3 figs. [Refs. in footnotes.]

Recovery from primary pneumonic plague is a noteworthy event and is very rare. The circumstances in the present case are somewhat unusual and their discussion turns on proof that the infection was primarily pulmonary, the treatment adopted, and the precautions taken for preventing spread of infection to contact persons. The patient was a doctor ; he had been engaged on plague investigation for 18 months and had had " five injections of plague vaccine over a period of six months, approximately one year previous to his illness." His illness began with malaise and chilliness, was accompanied by a hacking cough and quickly showed a temperature of 104°F. with blood-tinged sputum. One very important observation was that there were no buboes, nothing to suggest that this was pneumonia or septicaemic plague following local infection. Clinical evidence of pneumonia was an area of impaired resonance corresponding to an X-ray picture of a patch of infiltration. Plague bacilli were fully demonstrated in the sputum, morphologically, by culture and by animal injection. The author's approach to conclusion is cautious and may be quoted : " As far as I am aware this case is the first to be reported in which primary pneumonic plague has been treated by the use of sulfadiazine and the patient has recovered. However, the recovery cannot be attributed solely to a favourable action of this drug since other factors may have contributed to it," as for example his previous immunization, the rapidity with which treatment

was commenced and the extremely careful nursing which he received. He was treated in an oxygen tent, which also served to protect physician and nurses from infection. Some of the measures to prevent dissemination of infection were the wearing of masks, hoods, gowns and gloves by attendants, which fortunately, were entirely successful. *W. F. Harvey.*

DEVIGNAT, R. Sur un phénomène de dissociation chromogène de la souche virus-vaccin E. V. de Girard et Robic. [**Chromogenic Dissociation of the E.V. Strain.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, Jan., No. 3, 120–27.

Bibliographical references to dissociation of *Pasteurella pestis* are given under HADLEY [*Bulletin of Hygiene*, 1927, v. 2, 437], POLLITZER with WU LIEN-TEH *et al.* [this *Bulletin*, 1936, v. 33, 726] and other papers reviewed in *Tropical Diseases Bulletin* (1936–1940). The author, while preparing the batch of vaccine E.V. 70 from the 104th passage, found after 3 days at 26°C. that some of his Roux bottles gave in part an unusually heavy growth. This growth was examined microscopically and then subjected to control subculture test on glycerin-lactose agar and glucose agar. Isolated colonies of typical R and S types were obtained, both of which were of yellowish colour and both of which preserved their chromogenic characters. Further detailed tests were made of the morphological, cultural, biochemical and biological characters of this new strain, which resulted in the conclusion that this phenomenon represented a " chromogenic dissociation, perhaps even a mutation, giving colonies of typical R and S type." The strain is derived from *P. pestis* but its systematic classification is difficult, whether in the genus *Flavo-bacterium* or along with the bacillus of Malassez and Vignal. It is truly remarked that the precise systematic position of another organism allied to the plague bacillus—*P. pseudotuberculosis*—is not yet definitely settled. *W. F. Harvey.*

CHOLERA.

JENNINGS, R. K. **Starch Digestion of *Vibrio cholerae* in Strongly Aerated Media.** *J. Bacteriology.* 1945, Feb., v. 49, No. 2, 163–6. [14 refs.]

Methods and media used in this series of studies have already been abstracted in some detail in this *Bulletin* [1945, v. 42, 377]. In this continuation study the statement that *V. cholerae* rapidly digests starch with production of acid, but not gas, is investigated, and found to be true, but not wholly true. Starch (1 per cent.) was substituted for the glucose in the continuously aerated " salts C-D-medium " and its saccharification tested for at intervals, when—contrary to expectation—the *p*H " did not decrease at any time during growth." There was not at any time a significantly positive accumulation of glucose to give a reaction. The explanation offered is that " the glucose, if formed, must have been digested with considerable rapidity and the usual acid residue " also. A test of this explanation was instituted in which the glucose of the original medium " was replaced by (a) 1 per cent. sodium formate, (b) 1 per cent. sodium acetate and (c) 1 per cent. sodium lactate," with the result that no growth occurred in (a) but satisfactory growth developed in (b) and (c), especially in the (c) medium. The conclusion is reached that : " Heavy crops of *Vibrio cholerae* may be obtained in liquid media containing starch as the source of energy for reproduction, without accumulation of acid by-products, *provided* that the culture is efficiently aerated. Good growth may also be

obtained when sodium lactate is used as the energy food. Neither of these substrates is so satisfactory as the previously described BRF medium for vaccine production." *W. F. Harvey.*

BERNARD, P. N. & GALLUT, J. Recherches sur la toxine du vibrion cholérique. [**Cholera Toxin.**] *Ann. Inst. Pasteur.* 1945, Mar.–Apr., v. 71, No. 3–4, 65–82. [41 refs.]

PFEIFFER had originally contended that the toxin of the cholera vibrio was an intramicrobial endotoxin, not a diffusible exotoxin, and that it was set free only at the death of the organism. When METCHNIKOFF, ROUX and SALIMBENI demonstrated by their collodion sac technique that, rather suddenly, after 2 to 3 days, a fatal toxin diffused into the peritoneal cavity, they considered that they had provided proof of the existence of a cholera exotoxin. It is this contention which is opposed by the authors. Important contributions to the discussion were made when LANDSTEINER and LEVINE [this *Bulletin*, 1927, v. 24, 467] demonstrated the presence "in the cholera vibrio of a complex (glucides, fatty acid and phosphorus) capable of giving a polyoside haptene" and when BOIVIN, MESROBEANU and MESROBEANU (*C. R. Soc. Biol.*, 1933, v. 113, 490) isolated a complex and called it glucido-lipidic, because it was a combination of a phospholipid and a polysaccharide. This complex represented the chief element of the endotoxin and the somatic O antigen. This is the historical background of the discussion, which contends that the distinction between exotoxin and endotoxin is nowadays negligible, and that there is one complex cholera toxin, produced only at the death of the vibrio. It is capable of being split into a glucolipidic, antigenic constituent which is of too high molecular structure to traverse the collodion sac, and a non-antigenic protein-like constituent which can pass the sac and which, by its inability to give rise to any antitoxin, is probably not an exotoxin in the true definition of that word. One of the authors, GALLUT, has been a noted contributor [this *Bulletin*, 1943, v. 40, 910] to knowledge of the constitution and action of the glucolipidic complex. The cholera toxin has been prepared from one of the best out of 200 Indo-China strains, by growing it for 18 hours on glucose agar at *p*H 8; suspension in thrice-distilled water; centrifugation to obtain a vibrio deposit; resuspension in veal peptone bouillon; incubation at 37°C., and final subjection to prolonged centrifugation to furnish the toxic supernatant fluid. This toxin, at least equal to the best that can be obtained from cultures after several days, can be produced in 4 hours in glucose bouillon, in which the organisms become autolysed by the acidification set up from their fermentation of the glucose. The glucolipid constituent of the toxin produces the congestion and visceral necrosis of cholera, while the protein-like, but dialysable, constituent determines the symptom of hypothermy. *W. F. Harvey.*

GALLUT, J. & GRABAR, P. Recherches immunochimiques sur le vibrion cholérique. III. Mise en évidence de deux constituants toxiques de nature différente dans la toxine cholérique. [**Demonstration of the Two Different Constituents of the Cholera Toxin.**] *Ann. Inst. Pasteur.* 1945, Mar.–Apr., v. 71, No. 3–4, 83–92. [15 refs.]

Research into the nature of the cholera toxin has enabled the authors to define with precision the conditions favourable to rapid production of a very active toxin. The early work with intraperitoneal collodion sacs and dialysis was abandoned for fractionation by physico-chemical methods, such as ultra-filtration through membranes of known and graduated porosity. It may be assumed that the molecules of the antigenic gluco-lipidic complex are very

voluminous, as the solutions are opalescent, and the authors' first effort was directed to finding the terminal point of filtration, that is to say the most porous membrane which retained the complex entirely and allowed the remainder of the total toxin to pass. This ultrafiltrate is a limpid yellowish liquid giving a strong indole reaction and the chief reactions of proteins. True bacterial toxins are of protein nature, but should also be antigenic, which however, the ultrafiltrate is not.

The glucolipidic complex is toxic in the dose of 0·05 mgm. for a 15 gm. mouse; of 0·5 mgm. for a guineapig of 250 gm., intraperitoneally, and of 0·5 mgm. for a 2 kgm. rabbit intravenously. The pathogenic features of the toxic ultrafiltrate are very characteristic and are represented by hypothermy.

A summary of the characters of the two constituents of cholera toxin gives them as: I. *Glucolipidic endotoxin*—(1) 80–100 mμ; (2) neutralized by antiglucolipidic serum and by antiserum to total toxin; (3) productive of congestion. II. *Toxic substance of the ultrafiltrate*—(1) 4 mμ; (2) not neutralized by antiglucolipidic serum or by anti-serum to total toxin; (3) productive of hypothermy; (4) probably protide in chemical composition, possibly even protein. *W. F. Harvey.*

BACILLARY DYSENTERY.

Fortune, C. & Ferris, A. A. **Diarrhoeal Diseases in New Guinea.** *Med. J. Australia.* 1945, Apr. 7, v. 1, No. 14, 337–44. [18 refs.]

Among 2,849 patients with diarrhoea admitted to an Australian general hospital in New Guinea during a period of 18 months, 36·0 per cent. were proved to have bacillary dysentery, 1·4 per cent. amoebic dysentery, while the remainder were presumed on clinical and epidemiological grounds to have bacillary dysentery. [More careful bacteriological investigation in a smaller series reduced the proportion of cases in this last group.] Of 1,026 strains of dysentery bacilli isolated, 13·4 per cent. were *Bact. shigae*, 78·0 per cent. *Bact. flexneri*, 8·0 per cent. *Bact. ambiguum* (Schmitz), 2·4 per cent. *Boyd type IV*, and 0·2 per cent. *Bact. sonnei*. A detailed analysis was made of the bacteriology, symptomatology and treatment of 503 consecutive cases of diarrhoea. In this group 54 per cent. of 474 cases diagnosed as bacillary dysentery were confirmed bacteriologically by culture of both faecal specimens and rectal swabs (taken through the proctoscope: see same authors, *Bulletin of Hygiene*, 1945, v. 20, 183) on desoxycholate-citrate agar. The majority of infections were classified as mild or moderate; 18 per. cent. of the Shiga infections and 6 per cent. of the Flexner cases were severe. Among 35 consecutive patients with Shiga dysentery, sigmoidoscopic examination showed ulceration of the bowel in 20 and a strawberry-red oedematous mucosa in 13. The average stay in hospital for Shiga infections was 23·5 days and for Flexner infections 17·5 days.

Sulphaguanidine in large doses (initial dose 7 gm. followed by 3·5 gm. five times a day for 4 days and 3·5 gm. t.i.d. for 3 days) was given to all patients immediately after admission to hospital, and the results were uniformly good; Shiga infections responded better than Flexner infections. Only 30 cases (other than amoebic infections) had persistent or recurrent diarrhoea after a full course of treatment, and as these cases were bacteriologically negative and free of mucosal inflammation or ulceration, they were classified as "irritable bowel." Patients were discharged when sigmoidoscopic examination was normal and one rectal swab was bacteriologically negative. On this basis, 7 out of

179 (4·0 per cent.) bacteriologically proved Flexner infections were carriers and on the 14th day after commencement of treatment ; 9 other Flexner carriers at this stage were found still to have pathological changes in the bowel.

Surveys for carriers were made in three groups : (1) 120 healthy natives in a catering establishment where there had been no cases of diarrhoea for 3 months ; only one Flexner carrier was found ; (2) 50 men in a unit where Flexner infection was prevalent ; there were 5 Flexner excretors; of whom 3 were convalescent carriers ; (3) 133 men in a unit affected with epidemic diarrhoea ; 7 carriers were found ; 2 of *Bact. shigae* and 5 of *Bact. flexneri* ; 4 of these were convalescent carriers. Symptomless contact carriers responded well to sulphaguanidine, convalescent carriers less well : in 6 of 8 resistant cases in the latter category a course of sulphadiazine was effective. Some special points, including treatment, about amoebic dysentery are briefly discussed.

Robert Cruickshank.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

Hauer, A. & Deckert, K. Erfahrungen mit der Kultivierung von Darmprotozoen als einem Nachweisverfahren. [**Diagnosis of Infections by Culture of Intestinal Protozoa.**] *Deut. Tropenmed. Ztschr.* 1944, Feb.–Mar., v. 48, No. 3–6, 60–67, 3 figs.

Having found by experience that in many cases of intestinal protozoal infection a number of faecal examinations may have to be carried out on several days before such infections can be detected, the authors investigated the possibility of simplifying diagnosis by the employment of culture methods. They came to the conclusion that the best results were obtained with the Dobell-Laidlaw medium, consisting of a solidified serum base covered with Ringer-egg-albumin solution to which rice starch is added. It was found that in spite of buffering, the *p*H rapidly fell from the optimum of 7·4. This was remedied by pouring off the liquid and renewing it each day. After three or four days, owing to breaking up of the solid base, it was necessary to subculture to fresh tubes. In this way it has often been possible to detect both amoebic and flagellate infections which could not be discovered by direct microscopical examinations of the faeces. The identification of the organisms in cultures is, in many cases, easier than in the faeces, for a large number can be passed under review in a very short time. The differentiation of the culture forms requires some experience, but to help the uninitiated the authors describe the chief characters of the various amoebae which may appear. It is of interest to note that they support the view that the small race of *E. histolytica* is a separate species, *E. hartmanni*, and that through a number of subcultures it shows no tendency to assume the form of the typical large *E. histolytica*.

C. M. Wenyon.

Simonetti, C. Sindromi epigastriche e tiflo-appendicolari nelle coliti amebiche. [**The Epigastric and Appendicular Syndromes in Amoebic Colitis.**] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1944, v. 4, No. 4, 685–96. English summary (7 lines).

Dyspeptic symptoms associated with gastro-duodenal disturbances are common in patients with amoebic colitis ; these vary in degree between the " purely functional " and the " frankly organic ; " some are a mingling of the two. Among 2,400 whites (Italians ?) examined on account of digestive

disorders at the Asmara Hospital in 3 years 4 months to August 1944, there were 355 (15 per cent.) with duodenal ulcer and 101 (4 per cent.) with gastric ulcer; 315 (13 per cent.) had amoebic colitis. Seventy-eight (all males) had amoebic colitis and duodenal ulcer, and twenty-one (19 males, 2 females) had the amoebic colitis with gastric ulcer. Among 200 natives attending the hospital for the same causes during the same period, 35 had a duodenal and 5 a gastric ulcer, and 75 had amoebic colitis. Nine (all males) had duodenal ulcer and colitis; there were no cases of gastric ulcer and the amoebic colitis.

Next, appendicitis, or an appendicular syndrome—pain in the right iliac fossa with colic—is common in amoebic caecitis and colitis. Of the 2,400 Europeans examined, 318 (161 males, 157 females) had appendicitis; 45 males and 25 females had appendicitis and amoebic colitis. That is, 28 per cent. of the males with chronic appendicitis had amoebic colitis also, and 16 per cent. of 157 females. As regards the indigenous population attending the hospital, 10 out of 67 males with amoebic colitis suffered also from appendicitis, and 3 out of 8 women. Further, 10 of those with chronic appendicitis, 26 in number, were passing *Entamoeba histolytica* in their faeces. Of course, in some cases of acute appendicitis the form was the usual type and might have no connexion at all with the amoebic colitis, nor is it possible to say (in cases where operation was not performed) whether the chronic appendicitis was due to the *Entamoeba* or to the more usual causes. We can only say that chronic amoebiasis and chronic appendicitis may simulate each other and cannot always be differentiated [and may, of course, co-exist]. The concomitant incidence of the gastric and duodenal ulceration, and of appendicitis with amoebic colitis, is so high that it is more than likely that the conditions may be aetiologically connected. This aspect of the question is to be dealt with in another paper. *H. Harold Scott.*

Hunt, R. S. **Secondarily Infected Liver Abscess treated with Penicillin.** *Lancet.* 1945, Aug. 4, 138–41, 6 figs.

Luis Carri, E. Pseudo-epilepsia por giardiasis intestinal. [**Pseudo-Epilepsy due to Giardiasis.**] *Prensa Méd. Argentina.* 1945, May 18, v. 32, No. 20, 903–6. [19 refs.]

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Schwetz, J., with the collaboration of H. Baumann & M. Fort. Sur quelques foyers cryptiques de *Spirochaeta duttoni* du Congo Oriental. [**Some Cryptic Centres of *Spirochaeta duttoni* in the Eastern Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1943, Sept.–Dec., v. 23, Nos. 3–4, 219–36, 1 map.

During the course of a malaria expedition to the Eastern Congo in 1939, organized by the Royal Colonial Belgian Institute, the author took the opportunity of trying to find *Ornithodorus* in the various localities visited between Lake Kivu and Lake Albert. *Ornithodorus moubata* was found in five localities: Nyangezi, at an altitude of 1,650 metres; Nzulu and Kisenyi on the banks of Lake Kivu at 1,460 metres; and Bogoro and Géty, two districts overlooking Lake Albert, at 1,450 metres.

A total of 231 adults and 254 children from these five localities were examined for spirochaetes, with uniformly negative results.

The ticks from Nyangezi were examined for spirochaetal infection by Professor Roubaud, who, after several attempts, infected mice with them. Four lots of ticks were tested in Brussels. Two rats were inoculated with an

emulsion of ticks from Nzulu, and one showed spirochaetes on the 16th day. On the other hand two inoculated with ticks from Bogoro remained negative. Professor Roubaud also obtained infection with nymphs reared from *Ornithodorus* collected at Nzulu.

It is evident therefore, that Nyangezi, Nzulu, Kisenyi and Géty are centres of spirochaetal infection, even though the examination of nearly 500 local inhabitants failed to reveal any signs of infection. The author is of the opinion that these results support the view that the local population of centres of spirochaetal infection acquire immunity against the disease. *E. Hindle.*

Pirot, R. & Bourgain, M. Non-transmission héréditaire de *Spirochaeta persica* Dschunkowsky 1912, chez *Ornithodorus erraticus*. [**Failure of Hereditary Transmission of** *S. persica* **in** *O. erraticus*.] *Bull. Soc. Path. Exot.* 1944, v. 27, Nos. 1–2, 20–23, 1 chart. [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, June, v. 33, Pt. 6, 92–3.]

The usual vector of *Spirochaeta persica* appears to be *Ornithodoros tholozani*, Lab. & Mégn., but transmission has been effected experimentally by various ticks, including *O. erraticus*, Lucas. The experiments recorded in this paper were made with a strain of *S. persica*, thought to have originated in Persia, that has keen kept in the laboratory at Toulon for three years, is easily maintained in, and transmitted by, *O. tholozani*, and produces only a mild infection in guineapigs.

More than 80 examples of *O. erraticus* that had engorged in the second nymphal instar in June 1940 on guineapigs heavily infected with this spirochaete failed to transmit the infection to fresh guineapigs 7, 8 or 9 months later when they were in the next instar, and no infection was seen in any of the rodents on which the ticks were subsequently fed.

Chorine, V. & Colas-Belcour, J. Sur une souche tunisienne d'*Ornithodorus erraticus* réfractaire à l'infection par *Spirochaeta hispanica*. [**A Tunisian Strain of** *O. erraticus* **Refractory to** *S. hispanica*.] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 1–2, 24–34. [11 refs.]

Richter, C. P. **Incidence of Rat Bites and Rat Bite Fever in Baltimore.** *J. Amer. Med. Ass.* 1945, June 2, v. 128, No. 5, 324–6, 2 figs.

In an area of less than two square miles around the Johns Hopkins Hospital, Baltimore, U.S.A., there are many very poor houses that are infested by the brown rat, *Rattus rattus norvegicus*. The rats bite people at night while they are asleep, the great majority of the victims being infants under one year old. Most of the bites treated at the hospital were on the hands, head and feet, in that order of frequency.

The house distribution of the bitten persons suggested that the rat, having once tasted human blood, acquires an increased desire for it. An experiment in which rats were offered human blood with an alternative choice of other food and of water indicated that they had a strong preference for blood.

Of 65 persons from this area who were treated at the hospital for rat-bites, seven developed rat-bite fever [whether caused by *Spirillum minus* or *Streptobacillus moniliformis* is not stated]. *J. F. Corson.*

Wheeler, W. E. **Treatment of the Rat Bite Fevers with Penicillin.** *Amer. J. Dis. Children.* 1945, Apr., v. 69, No. 4, 215–20, 4 charts. [13 refs.]

Wheeler describes the treatment with penicillin of four cases of rat-bite fever, three due to *Streptobacillus moniliformis* and one to *Spirillum minus*. He has

developed a satisfactory technique for the isolation of *Streptobacillus moniliformis* from the blood: at least 8 cc. of blood are inoculated into 50 cc. of broth, and the culture incubated at 37°C. in an atmosphere enriched with CO_2. The flask is examined daily in a strong cross-light for the presence of "cotton ball" colonies; if present, these are transferred with a pipette to chocolate agar for subculture and to a slide for Gram staining. After incubation in CO_2, the subculture is used to inoculate a plain agar plate and a blood agar plate, and to make a smear for staining with Giemsa. The characters required for diagnosis of *Streptobacillus moniliformis* are: typical colonies in broth, Gram-negative pleomorphic organisms in the smear, failure to grow on plain agar, and scanty or no growth on blood agar.

Streptobacillus moniliformis was isolated from blood taken from three children—aged 5 weeks, 7 weeks, and 6 months—who had been bitten by rats. One of the children showed a marked arthritis, one a fine macular rash, and one showed marked respiratory distress, and later developed an abscess over the sternum from which viable *Streptobacillus moniliformis* were recovered three days after starting penicillin. In two children the temperature was raised, in the third it was subnormal; it returned to normal in all cases 2–4 days after the start of penicillin, though in one child only after three blood transfusions. Penicillin was administered intramuscularly at the rate of 5,000 units every two or three hours for nine days. The clinical progress was satisfactory in all the cases.

A fourth child, aged three months, had also been bitten by a rat, was febrile, and showed a macular rash; unlike the other three his local lesions were markedly inflamed. His blood did not yield *Streptobacillus moniliformis* on culture, but two mice which had been injected with 0·5 cc. showed spirilla morphologically resembling *Spirillum minus* on the 15th day. The response to penicillin, 5,000 units three-hourly, was dramatic, the temperature falling to normal in nine hours. *R. E. O. Williams.*

YAWS.

Guimarães, F. N. Bouba ("Framboesia, pian, yaws). Tratamento pela penicilina das lesões terciárias: ulcerações gomosas, periostites, osteites áreas de rarefação óssea e gangoza ("Rhinopharyngitis mutilans"). (Nota prévia.) [**Penicillin in the Treatment of Tertiary Yaws.**] *Brasil-Medico.* 1945, Mar. 17, 24 & 31, v. 59, Nos. 11, 12 & 13, 89–91, 6 figs. English summary.

Brief notes are given of six patients presenting lesions of tertiary yaws—gummata, periostitis, osteitis and gangosa—treated with injections (usually gluteal) of penicillin. The total dosage ranged between 48,000 units given during 20 days to a child of five years with periostitis, and 558,000 units over 7½ months to a lad of 16 years with boomerang leg and gummatous ulcers. Ten-day rest intervals were given from time to time (36 days altogether in the last case). The treatment in this patient comprised 1,200 units daily for 90 days; 2,400 units for 27 days; 3,600 units for 23 days; 4,800 for 43 days; and 9,600 for 10 days.

The gangosa patient was a woman of 26 years. She was given 400 units thrice daily for six days, then 800 t.d. for 39 days, then 1,600 similarly for 12 days; altogether 158,400 units [not 164,000 as stated]. The gangosa

cleared up but a residual goundou was observed. Cure was obtained in all cases with ulceration and periostitis, but the actual bony changes persisted.

H. Harold Scott.

CHARTERS, A. D. **Foot Yaws.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, July, v. 38, No. 6, 461–2, 6 figs. on 1 pl.

A report of a case.

LEPROSY.

SUÁREZ, J. La lepra en Bolivia. [**Leprosy in Bolivia.**] *Bol. Oficina Sanitaria Panamericana.* 1944, Nov., v. 23, No. 11, 966–74, 1 map.

In accordance with a resolution passed by the National Antileprosy Service in April 1942 a census of lepers was undertaken in Bolivia. The first team explored the Departments of Beni, Panda, and Santa Cruz, and they discovered 19 foci, and in them 56 lepers and 212 contacts among 6,000 persons examined.

From May to September 1943, a second team was working in six Departments: Santa Cruz, Beni, Cochabamba, Tarija, Potosí, and Chuquisaca. This second Commission discovered 64 new foci, 161 lepers and 497 contacts. Thus the two Commissions found 83 foci, 217 lepers and 709 contacts.

The author then takes each of the Departments in turn, naming the foci and the numbers of cases and contacts in each focus. Here it must suffice to give the numbers in the several Departments; for readier study the facts presented in the letterpress have been brought together in tabular form.

Department	Foci	Lepers	Contacts
Santa Cruz...	30	70	226
Beni	14	45	132
Tarija	15	33	144
Chuquisaca	10	39	152
Cochabamba	6	22	55

In Chuquisaca there were another six probable foci. As regards Potosí the position is uncertain; only one actual patient was seen and he had come from the Province of Charcas. He was isolated in the local hospital but ran away. The information in other respects is quite vague, the author stating that "there are possibly many more cases . . . . and several localities may be foci" of the disease.

So much for the census aspect. Epidemiological study shows that the foci may be graded: active foci are those in which more than 60 per cent. of the cases are florid (lepra abierta); stationary, where half or less of the cases are of the types L1, L2 or L3; and inactive or becoming extinct, where more than 70 per cent. are of the nervous types or *formes frustes*. Further analysis showed that 53 per cent. were autochthonous, 12 per cent. imported; the source of the remaining 35 per cent. was not known. Ninety-two per cent. were natives,

6 per cent. half-caste, and 2 per cent. white ; 87 per cent. were males, 13 per cent. females. With such small numbers the age-grouping does not convey much information, but the following may be useful :—

Age in years	Males	Females
0–4	0	1
5–9	8	2
10–14	13	4
15–19	45	8
20–29	65	3
30–39	33	4
40–49	15	3
50–59	10	3
60–	0	0

The estimated population being taken as 3,000,000, the leprosy incidence is stated to be 70·5 per 100,000. Contact is largely extra-domiciliary, 77 per cent., as compared with 23 per cent. in the home.

To deal with the situation the Antileprosy Service intends to establish two colonies of agricultural type, one in the Michel district where periodic flooding does not occur and medical and other aid can be easily given ; the other at Los Negros estate in Florida Province. Neither of these is an endemic centre, the land is suitable for agriculture, water supply is adequate and of good quality and access is by good roads. Next, eight mobile dispensaries are to be provided, each to work in its own determined range. These will continue the census, treat the sick, examine periodically the contacts and attend generally to the health education of the people. Propaganda work will also be carried out.

H. Harold Scott.

Mouritz, A. **A Brief World History of Leprosy. Hawaii ; U.S. America ; Philippines; Malaya ; Fiji ; China ; India ; Europe.** 139 pp., 31 illustrations. Revised 1943. Honolulu, Hawaii : Hawaiian Printing Co., Ltd. [31*s.* 6*d.*]

Mudrow, Lilly & Schultz, F. Die Rattenlepra unter Vitaminmangel und bei chronischer Sapotoxinverabreichung. [**The Influence of Vitamin Deficiency and of Prolonged Administration of Sapotoxin on Rat Leprosy.**] *Zent. f. Bakt.* I. Abt. Orig. 1943, Dec. 11, v. 151, No. 1, 50–59, 3 figs. [10 refs.]

The main part of this paper deals with the effects of vitamin B_1 deficiency on the development of inoculated rat leprosy. The results were largely negative, for vitamin deficiency did not appear to increase the generalization of infections with rat leprosy in the case of either B_1, biotin or pantothenic acid, nor was the spread of the rat leprosy bacilli through the system of the animals influenced. No specific effect of the vitamin deficiency on the pathological process could therefore be established, though some general influence may have been exerted in the direction of aggravating the disease. These animal tests may indicate the likelihood of similar influence in human leprosy. The last part of the paper gives data indicating that the supply of sapotoxins to rats infected with rat leprosy does not intensify the severity of the disease. *L. Rogers.*

HELMINTHIASIS.

Cawston, F. G. *Bulinus forskalii* (**Ehrenburg**) **as a Factor in the Spread of Schistosomiasis.** *South African Med. J.* 1945, May 12, v. 19, No. 9, 155.

In this note the author emphasizes the fact that this snail is to be found in parts of South Africa, and must be taken into account.

Schwetz, J. & Dartevelle, E. Le problème des mollusques vecteurs de la bilharziose au lac Albert. [**The Molluscan Vectors of Schistosomiasis round Lake Albert.**] *Ann. Soc. Belge de Méd. Trop.* 1944, June 30, v. 24, Nos. 1–2, 58–68, 6 figs. on 1 pl. [22 refs.]

Schwetz, J. & Dartevelle, E. Répartition géographique des "Planorbidae" (*Planorbinae* et *Bulininae*) au Congo belge, d'aprés les collections malacologiques du Musée de Tervuren, 1943. [**The Distribution of** *Planorbis* **and** *Bulinus* **in the Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1944, Sept. 30, v. 24, No. 3. 147–66, 3 maps. [10 refs.]

Almy, T. P. & Harper, J. G. M. **Banti's Syndrome apparently due to Infection with** *Schistosoma mansoni.* *J. Amer. Med. Ass.* 1944, Nov. 11, v. 126, No. 11, 703–5, 4 figs.

A case of very prolonged development of symptoms, the patient being a man of 44 years who had probably contracted his infestation with *S. mansoni* at latest when he was 19 years of age and perhaps earlier. He was an Arab, born near Aden in 1899; he had been in the British Navy and the merchant service for five years from the age of fifteen, and since 1919 had not left the United States. Splenomegaly had been observed when he was operated on for hernia at the age of 42. Two months before his present admission to hospital he noticed swelling of his abdomen and legs and shortness of breath on slight exertion. On admission the heart was normal, the liver edge was 7 cm. below the costal margin at the mid-clavicular line and the tip of the spleen was felt at the level of the umbilicus. Blood examination showed red cells 3,600,000, white 4,000 per cmm. with 12 per cent. eosinophiles. Wassermann reaction was negative. After three weeks' treatment with iron and liver extract the erythrocytes had increased to 4,900,000, while the leucocytes remained the same in total, but eosinophiles were down to 4 per cent. He was then treated with Fuadin, but though he tolerated the drug well it had no effect on the liver or spleen which, 10 weeks after cessation of treatment, remained the same as before. There seems to be no doubt that infestation had occurred at his place of birth, which he had left 30 years ago. [It is true that no other cause was found to account for the enlargement of the liver and spleen, but the tissue of neither organ was examined by biopsy, and, on the other hand, nothing certain is known regarding the aetiology of Banti's syndrome. It would, perhaps, be safer to call this a long-standing case of Schistosomiasis mansoni associated with the signs and symptoms of Banti's syndrome.] *H. Harold Scott.*

Alves, W. **Intensive Treatment of Schistosomiasis with Antimony. (Preliminary Note.)** *South African Med. J.* 1945, May 26, v. 19, No. 10, 171–2.

The author was led to make trial of this method of intensive treatment first, because of the reported success of a similar method with arsenic in syphilis, and, secondly, because schistosomiasis is a very important problem in Southern Rhodesia. He used a preparation of sodium antimonyl tartrate (S.A.T.) in

ampoules containing 1 or 2 grains and the injection was made up to 10 cc. with 5 per cent. glucose saline. The calculated dose was, approximately, 12 mgm. per kilo. body-weight, and was administered in 7–8 doses over a period of 30 hours, with 16–18 hours' break after the first day of treatment. For example, a young adult weighing 55 kgm. was given 650 mgm. as follows: 65 mgm. at 9.30 and 11.30 a.m. and at 2 p.m.; 130 mgm. at 4.30 p.m. At 8.30 a.m. next day (*i.e.* after a 16 hours' interval) 130 mgm.; at 10.30 a.m., 12.30 and 3.30 p.m., 65 mgm. each time, the whole being thus spread over 30 hours. Each intravenous injection was given slowly, 5–6 minutes being taken over it. Reports of the results have, so far, been very good and most encouraging. The ova disappeared or, if found, were not viable, after a couple of days. Brief notes of five patients are given and a reference to a sixth who has been lost sight of. It may, as the author acknowledges, be too soon to claim a cure, for a longer follow-up is needed, but the method in his hands has had no troublesome complications and is well worth, and will doubtless receive, more extensive trial. *H. Harold Scott.*

VIDELA, C. A. & SCODELLER, J. A. Distomatosis Hepatica. [**Infestation with** *Fasciola hepatica.*] *An. Policlin. Enf. Infecciosas del C. A. Videla, Hospital F. J. Muñiz.* Buenos Aires. 1942–44, No. 4, 144–63, 1 fig. English summary (3 lines).

APPLEBAUM, I. L. & WEXBERG, L. E. **Eosinophilia in Cerebrospinal Fluid.** *J. Amer. Med. Ass.* 1944, Mar. 25, v. 124, No. 13, 830–31, 1 chart. [17 refs.]

"1. A case with the findings of eosinophilia in the spinal fluid and manifestations of acute cerebrospinal meningitis was observed.

"2. The syndrome closely resembled cases of cysticercosis of the central nervous system previously described and was considered the most probable diagnosis.

"3. The condition is more common than is generally recognized and in suspected cases such special procedures as sedimentation of the spinal fluid in a search for eosinophils, and intradermal and precipitin tests are recommended."

[Seventeen references are given to the literature of this subject.]

SELMAN, D. **Eosinophilia in Cerebrospinal Fluid. Report of Case.** *Bull. U.S. Army Med. Dept.* 1945, Mar., No. 86, 121–2, 1 fig.

The patient was a man with signs of meningeal irritation, and slight fever. On the day after admission the blood showed 5 per cent. of eosinophils in a total leucocyte count of 7,400 per cmm. and the blood eosinophils never exceeded 5 per cent. during the illness. On the day after admission the cerebrospinal fluid was hazy and colourless, with a pressure of 12 mm. Hg.; it contained 480 cells per cmm., of which 71 per cent. were eosinophils and 27 per cent. were lymphocytes. The Wassermann and colloidal gold tests were negative. On the third day there was no nuchal rigidity and the cerebrospinal fluid showed 670 cells per cmm. with 78 per cent. of eosinophils. On the 21st day it showed only five cells per cmm., of which one was an eosinophil. On the 13th day the subject was discharged to duty. The treatment is not described.

Examination of the stools for parasites at intervals were all negative. The author refers to literature recording the following causes of cerebrospinal eosinophilia: neurosyphilis, "experimental serum meningitis," "therapeutic intraspinal malarial blood injections," cerebral echinococcosis and cysticercosis.

He concludes that cerebral cysticercosis was the most likely cause of the eosinophilia observed in this subject, but lack of antigen prevented intradermal, precipitin and complement-fixation tests for the detection of this parasite or of *Echinococcus*. The fact that the illness came on six days after the last of three prophylactic injections with typhus fever vaccine suggests to the author that these injections might cause cerebrospinal eosinophilia, and he suggests that this problem should be investigated. [See also this *Bulletin*, 1942, v. 39, 705.]

G. Lapage.

Howorth, M. B. **Echinococcosis of Bone.** *J. Bone & Joint Surgery.* 1945, July, v. 27, No. 3, 401–11, 7 figs. [75 refs.]

"The development of our knowledge of echinococcus disease has been outlined, and its etiology and distribution have been described. The disease is rare in this country, but not uncommon in other areas, and its increase may be expected because of conditions growing out of the War. Its diagnosis, especially in bone, is not difficult, if its possibility is realized, and if proper laboratory tests and roentgenograms are made. Treatment has been unsatisfactory to date. Marsupialization or sterilization of the cyst sometimes may be successful. Roentgen radiation has failed. Removal of the entire diseased area has removed the disease, but is mutilating. Insertion of bone chips will not be successful, unless the disease has been eradicated."

Lisbôa, A. Estrongilose renal humana. [**Renal Strongylosis in Man.**] *Brasil-Medico.* 1945, Mar. 17, 24 & 31, v. 59, Nos. 11, 12 & 13, 101–2.

Infestation of man by *Dioctophyma renale* is exceedingly rare. Only nine cases have been recorded before this. The patient was a white woman, 54 years of age, a resident of Maranhão, a Province of Brazil, who had suffered from pruritus vulvae for the past nine years. Suddenly one day, during micturition, she felt a stoppage "as if a stone had blocked the urinary passage"; on straining, the flow returned and a worm was passed. There has been no further trouble and the pruritus has ceased. The worm was sent for examination to Dr. Carlos Porto, who diagnosed it as a male *Dioctophyma renale* [*Eustrongylus gigas*]. This is the largest of the parasitic nematodes; the female may attain a length of 3 feet and the thickness of a man's finger; the male is only one-fourth to one-third the length of the female. The life-history is not known; the infestation is more commonly found in dogs and is thought to be acquired by ingestion of raw fish.

H. Harold Scott.

Tsuchiya, H. & Reller, Helen. **A Case of Trichostrongylus Infection with Notes on the Identification of Ova.** *J. Lab. & Clin. Med.* 1945, Mar., v. 30, No. 3, 262–6, 1 fig.

Infestation with *Trichostrongylus* is exceedingly rare in the United States, but in India it has been reported in 9–25 per cent. of the population of the sheep- and goat-raising areas [this *Bulletin*, 1942, v. 39, 775], and in Japan in 32·3 per cent. [see also this *Bulletin*, 1937, v. 34, 457, and 1939, v. 36, 845].

The authors now report the finding of *Trichostrongylus* eggs in the faeces of a man who died of malignant disease in the United States; attempts to culture the worms were unsuccessful, so that the species could not be determined.

Discussing the identification of the eggs of *Trichostrongylus*, the authors describe them as being much longer and slightly wider than those of hookworms, which they may resemble. A table of measurements of 25 *Trichostrongylus* eggs shows that they measured 81–97 microns long by 40–51 microns broad, average

86 by 43 microns. The shell membrane of the *Trichostrongylus* eggs is thicker and more greenish and lustrous than that of hookworm eggs. MAPLESTONE [this *Bulletin*, 1942, v. 39, 775] likened their shape to that of the eggs of a bird. In fresh stools *Trichostrongylus* eggs show advanced segmentation of the contents, 16 to 24 cells usually being present. *Haemonchus contortus* is another rare parasite of man and its eggs may cause confusion. They cannot be distinguished from those of *Trichostrongylus* and the only method of identifying this species is by cultivating the infective larvae or by finding the adult nematode. The eggs of *Strongyloides stercoralis* may also be found, but these are smaller and have a thinner shell membrane which is less greenish and less lustrous ; in the fresh stool the eggs of this species contain an embryo.

The eggs of *Heterodera radicicola* may appear in human stools after ingestion of vegetables in which this nematode is parasitic. The eggs of this species have a unilateral flattening or a slight concavity and their ends are rounded ; but distorted eggs may be incorrectly diagnosed. They may disappear when the subject is put on a diet free from vegetables.

The authors stress the importance of careful stool examinations for the differentiation of the eggs of *Trichostrongylus* from those of the hookworms.

G. Lapage.

CRAM, E. B. & HICKS, D. O. **The Effect of Sludge Digestion, Drying and Supplemental Treatment on Eggs of** *Ascaris lumbricoides*. *Proc. Helminth. Soc.* Wash. 1944, v. 11, 1–9. [Summary taken from *Vet. Bull.* 1945, May, v. 15, No. 5, 156. Signed T. E. GIBSON.]

Eggs of *A. lumbricoides* originating from man and swine were introduced into sewage taken from a town main and the sewage seeded with ripe sludge, generally in the proportion of four parts of settled sewage to one part of ripe sludge. To ten parts of ripe sludge was added daily for 30–60 days one part of fresh settled sewage, giving a yield of 60–72 litres of sludge at the end of the observation period. The effects of digestion were observed for 2–6 months, and then the sludge was poured for drying into wooden frames containing layers of gravel and sand of varying depths. The different lots of sludge were dried by exposure to constant temperatures of 86° and 68°F. and to the varying temperatures of the laboratory, a greenhouse, and a porch roof. Viability of the eggs was judged by the development of active embryos.

Eighteen lots of eggs were placed in digesting sludge and practically none developed. The eggs were very resistant to the digestive process and an average of 70 per cent. of all eggs exposed at different temperatures were viable during the first three months, after which a sharp drop in viability occurred. At the end of six months, however, about 10 per cent. of the eggs were still viable. Repetition of the sludge digestion appeared to be no more deleterious to *Ascaris* eggs than was continuous sludge digestion. It was found that under the aerobic conditions found in activated sludge, active embryos developed in *Ascaris* eggs which had been unsegmented when they were introduced into the sewage. Subsequent exposure to anaerobic sludge digestion showed that embryonated eggs survive anaerobic digestion for periods longer than those usually allowed for sludge digestion, although they seem to be less resistant than non-embryonated eggs.

Six lots of digested sludge were dried in the greenhouse and 13 cakes of sludge were dried outside. Variable viability was noted under these varying conditions, but it appears that *Ascaris* eggs cannot survive a reduction of moisture content to below 5 per cent. Storage of pulverized, dried sludge containing 30·7 per cent. of moisture at 68°F. in a tightly covered glass dish did not influence the viability of *Ascaris* eggs during 44 days. Subsequently the powdered sludge

was left in a loosely covered dish which allowed slow drying, and 71 days later the moisture content was 4·5 per cent. and no viable eggs could be recovered. Heating the sludge to 50°C. for 20 min. killed about 50 per cent. of the viable eggs present and heating to 103°C. killed all the *Ascaris* eggs present. Fumigation of eggs in sludge and sand with methyl bromide for 24 hours destroyed those eggs which had not started their development, but had little effect on partially or completely developed eggs.

ENGLEHORN, T. D. & WELLMAN, W. E. **Filariasis in Soldiers on an Island in the South Pacific.** *Amer. J. Med. Sci.* 1945, Feb., v. 209, No. 2, 141–52, 4 figs.

An account is given of the early symptoms and signs of illnesses which were diagnosed as filariasis, occurring among American soldiers stationed in an island in the eastern part of the South Pacific Ocean. Neither adult nor larval filariae were found in the patients, but filariasis was very common among the natives of the island, there was close contact between the troops and the natives, and the commonest mosquito, present in great numbers, was *Aëdes scutellaris*.

The shortest period between possible exposure to infection and the development of symptoms was 3 months, mild symptoms appeared most frequently after 5 months, and severe symptoms after 8 months.

The earliest symptoms were malaise, insomnia, anorexia, nausea, vomiting and pain in various parts of the body; after about 2 weeks, pain, tenderness and swelling of the scrotum and spermatic cord developed and, in some patients, signs of acute lymphadenitis and acute lymphangitis appeared, usually in the upper arm and the thigh, and spread peripherally.

All the patients had funiculitis, 69 had orchitis, and 22 had epididymitis, while lymphadenitis was present in 9, acute lymphangitis in 8, and acute cellulitis in 9. Some of the patients had transient, soft, non-suppurative swelling in the arm, hand, leg or upper eyelid.

In accordance with the policy of the Army the men were evacuated to the U.S.A.

A short account, illustrated by photographs, is given of filariasis among the natives. *J. F. Corson.*

GERMAN, W. M. **Observations on the Microfilaria of *Onchocerca volvulus* with Silver Stains.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 129–36, 8 figs.

The illustrations of the larvae of *Onchocerca* in recent textbooks are criticized, their lack of detail being due, in the author's opinion, to the use of routine stains; he has found that a silver staining method gives a better contrast between the larvae and their surroundings and shows more anatomical detail.

The following watery solutions are used: (*a*) 2 per cent. $AgNO_3$; (*b*) ammoniacal silver carbonate, prepared as follows:—to 5 cc. of 10 per cent. silver nitrate add 15 cc. of 5 per cent. Na_2CO_3, then add strong ammonia solution drop by drop until the white precipitate is dissolved, and add a few extra drops, then add distilled water to 75 cc.; (*c*) 1 per cent. formol; (*d*) 5 per cent. sodium hyposulphite.

Frozen sections are placed successively in the following: (1) distilled water (twice); (2) in (*a*) and heat at 60–70°C. until the sections become faintly yellow (15–20 minutes); (3) distilled water (twice); (4) in (*b*) for 3–5 minutes; (5) distilled water for 1 minute; (6) in (c) for 1 minute; (7) distilled water; (8) in (d) for 1 minute; (9) distilled water, drain, blot, dehydrate, clear in creosote, and mount in 'clarite x.' The larvae are stained black in a yellow background.

The author discusses the morphology of the larvae as shown by this silver method and describes their position in the nodules ; he concludes that they leave the nodule by the perivascular spaces. [The morphology of the larva of *O. volvulus* is well shown in a paper by Fülleborn and Simon, *Arch. f. Schiffs- u. Tropen-hyg.*, 1913, v. 17, Beiheft 9 (see this *Bulletin*, 1914, v. 3, 100).]

J. F. Corson.

Rodhain, J. Contribution à l'étude des ganglions inguinaux dans l'adénolymphocèle et l'éléphantiasis du scrotum au Congo Belge. [**The Inguinal Glands in Adenolymphocele and Elephantiasis in the Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1943, June 30, v. 23, No. 2, 91–111, 6 figs. [10 refs.]

In a previous paper (*Ann. Soc. Belge de Méd. Trop.*, 1936, v. 16, 253) the author described the histological appearances of lymphatic glands removed from African natives of the Belgian Congo who were infested with *Onchocerca volvulus* ; two of those patients had " adenolymphocele " and one had scrotal elephantiasis. In the present paper detailed descriptions are given of the conditions observed in lymphatic glands and pieces of skin excised from Congolese natives with " adenolymphocele " or scrotal elephantiasis. Some of the specimens came from Niangara in the Uele area, where nearly the whole of the population has onchocerciasis, while others came from Coquilhatville, where onchocerciasis exists but is less common.

The glands and skin showed fibrosis of varying degree, especially in cases with onchocerciasis ; in some glands the lymphatic channels were dilated but no large spaces were seen. The author thinks that further observations, with more associated details, are needed and that comparisons should be made between these cases in Central Africa and similar conditions associated with filariasis caused by *Wuchereria bancrofti*.

The meaning of the term " adenolymphocele " is discussed ; Stephens and Yorke (" The Practice of Medicine in the Tropics " by Byam and Archibald, 1923, v. 3, 1928) are quoted as stating that it " apparently implies dilatation of the sinuses in a lymphatic gland." Dubois (*Bull. Acad. R. de Méd. de Belgique*, 1940, VI ser. v. 5, 364) regards it as an unsuitable term, and the author thinks it is used for more than one pathological condition. *J. F. Corson.*

Bell, S. D., Jr. & Brown, H. W. **Studies on the Microfilarial Periodicity of *Litomosoides carinii*, Filariid Parasite of the Cotton Rat.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 137–40, 3 figs.

Litomosoides carinii, a filariid parasite of the thoracic cavity of the cotton rat, *Sigmodon hispidus*, and of various other rodents, appears to have been given various names : *Filaria carinii*, *F. patersoni*, *Litomosoides sigmodontis*, and *Micropleura sigmodoni*.

The authors examined thin blood smears stained with alum haematoxylin and observed the following characters : the microfilaria has a sheath about 100μ long, a clear area behind the anterior end of about 3–5μ and the nuclei reach to the end of the tail in most cases.

Thick smears were made with 3·5 cmm. of the tail blood of six cotton rats, every four hours for 48 hours, and stained with Giemsa's stain, and the microfilariae were counted. Although considerable variations in numbers were found, there was no obvious nocturnal or diurnal periodicity. To determine whether there was any periodicity over longer periods, one rat was examined every 12 hours for nine days and every 24 hours for 20 days ; no regular cyclical variation was found.

The considerable variations which occur make this filaria difficult for testing the effects of chemotherapy, but for testing the killing power of drugs on the adult filariae the cotton rat is a good experimental animal [see this *Bulletin*, 1944, v. 41, 772; 1945, v. 42, 136]. *J. F. Corson.*

Rodhain, J. Présence de *Microfilaria streptocerca* dans les régions de Lisala et de Basankusu (Congo Belge). [*Microfilaria streptocerca* **in the Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1943, Sept.–Dec., v. 23, Nos. 3–4, 203–8, 6 figs. on 2 pls.

Agamofilaria streptocerca was found, in 1939, in the skin of three natives of the Belgian Congo; two of the natives were in Lisala and one in Basankusu. This larval form was also found in Nepoko, in the Belgian Congo, in 1938 by Dubois and Vitale [this *Bulletin*, 1940, v. 37, 306]. *J. F. Corson.*

DEFICIENCY DISEASES.

Briggs, A. P., Singal, S. A. & Sydenstricker, V. P. **A Study of Nicotinic Acid Restriction in Man.** *J. Nutrition.* 1945, May 10, v. 29, No. 5, 331–9, 1 fig. [20 refs.]

"Two subjects, each of whom previously had been a pellagra patient, restricted themselves to a diet low in trigonelline and providing only about 3 mg. of nicotinic acid daily, one for a period of nine weeks and the other for 42 weeks.

"Each had minimal lesions of nicotinic acid deficiency at the start, but in neither was there any significant development in the direction of pellagra.

"The nicotinic acid excretion of one remained low throughout the study; the other remained at a normal level.

"The trigonelline output in each case dropped to a low level within 3 weeks, but showed no tendency to fall to a lower level with prolonged restriction.

"Niacin tolerance tests in each case were interpreted to indicate a mild state of deficiency.

"Tests for the fluorescent substance F_2 were zero at the start as well as at the close of the periods of restriction.

"It is suggested that the failure in the development of pellagra may have been due possibly to intestinal biosynthesis of nicotinic acid, and possibly to the fact that the diet contained little corn.

"Apparently, under the conditions of our study, the 3 mg. daily of the diet provided an intake somewhere near the minimal niacin requirement."

Rachmilewitz, M. & Braun, K. **Electrocardiographic Changes and the Effect of Niacin Therapy in Pellagra.** *Brit. Heart J.* 1945, Apr., v. 7, No. 2, 72–80, 4 figs. [13 refs.]

The authors (writing from Jerusalem) produce further observations upon electrocardiographic changes in patients showing clinical signs of nicotinic acid deficiency, which were eliminated by the administration of this substance, but not by vitamin B_1. Of the 27 subjects, 22 had typical skin lesions of pellagra; 10 showed, as well, evidence of thiamin deficiency, such evidence according to the authors being pains in the calf muscles, paraesthesia, muscular weakness and cramps as well as "objective findings indicating peripheral neuritis," but not one patient had disturbances of cardiac function and none a beriberi

heart. [Here the authors do not seem to be very clear—the one condition which is due to a thiamin deficiency is the beriberi heart, while the relationship between the so-called peripheral neuritis and vitamin B_1 is doubtful.]

The changes in the E.C.G. considered to be due to nicotinic acid deficiency (16 cases) were alterations of the final deflection of the ventricular complex—alteration of the S-T segment or of the T wave, since, though similar changes may be seen in beriberi, arteriosclerosis, myxoedema, etc., they appeared to clear up after the exhibition of 300 to 500 mgm. of nicotinic acid per diem. None of these cases showed any clinical or radiological evidence of cardiac abnormality.

In two cases in which there was an associated protein deficiency, the condition did not respond until the blood protein had been restored to normal. Nine cases showing well marked dermal manifestations of pellagra without obvious signs of involvement of visceral organs tended to give normal E.C.G.

H. S. Stannus.

COMERFORD, C. & KIRMAN, B. H. **Pellagra in a Morphine Addict.** *Brit. Med. J.* 1945, July 14, 44–5.

CARLEY, P. S. **History of Pellagra in the United States.** *Urologic & Cutaneous Rev.* 1945, May, v. 49, No. 5, 291–303. [147 refs.]

HAEMATOLOGY.

INDIA. ARMY PATHOLOGY ADVISORY COMMITTEE GENERAL HEADQUARTERS (INDIA). **Report on Investigations on Anaemia in the Indian Soldier from the Anaemia Investigation Team General Headquarters (India). September 1943–January 1945** [HYNES, M., Officer in Charge]. 59 pp., 18 figs. [52 refs.] 1945. New Delhi: Printed by the Manager, Government of India Press.

Anaemia in the Indian soldier was a major medical problem on the Indo-Burma front during 1943. An investigation into the cause of this anaemia was undertaken between September 1943 and January 1945.

The first section of the report gives a review of the literature on anaemia in India. Over fifty papers, to which the references are given, have been consulted. It is a useful summary.

Haemoglobin surveys of several groups of soldiers, pioneers, and recruits were carried out. A haemoglobin level of not less than 14 gm. per 100 ml. was taken as " satisfactory " and one of less than 11 gm. as indicating anaemia of a sufficient degree to justify hospitalization. Two intermediate groups were also recognized, " doubtful "—13 to 13·9 gm. and " mild " anaemia—11 to 12·9 gm.

The reviewer has tabulated the findings (below); the percentages are calculated to the nearest whole figure.

The possible causes of the relatively low haemoglobin in most of the Indian groups is discussed. The effects of hookworm infection, dietary deficiency, malaria, length of service, and altitude are considered. Statistically significant evidence for the effect of hookworm infection is found, but the authors of the report are disinclined to give this infection the importance it appears to deserve, for several reasons that are stated. [The reviewer questions the validity of

	Percentage in each group				
	No. of persons	Anaemic	Slightly anaemic	Doubtful	Satis-factory
Imphal area (3,000 to 10,000 feet)					
Madrasi Pioneers	100	17	29	24	30
Bengal Pioneers	60	0	3	5	92
British other ranks	200	1	6	14	80
Mahrattas & Jats	500	2	8	12	78
Gurkhas	210	5	22	25	48
Patiala Brigade	100	7	24	29	40
Peshawar District (1,100 feet)					
North West Indians :					
February	1,119	5	32	33	30
May	189	3	8	25	63
Madrasis	200	1	27	36	37
Brit. other ranks	195	0	9	32	60
Landi Kotal (3,500 feet)					
Punjabis	197	2	17	28	53
Bhairab Naths	200	1	3	19	78
Kashmiris	200	2	5	14	80
Rawalpindi					
Recruits	600	7	19	19	55

excluding hookworm infection as the cause of anaemia because of the absence of (i) demonstrable hookworm infection in certain anaemic individuals of a hookworm-infected group, and (ii) anaemia in some relatively heavily infected persons.] The longer the service the less the anaemia, but this fact may, of course, also be correlated with hookworm infection.

A more detailed blood examination of recruits was made, and it was found that the anaemia was mostly of the ortho or hypochromic types.

It was found that iron administration raised the haemoglobin level, often to a remarkable degree, in all the substandard groups, and in most of the individuals of these groups, even when the haemoglobin percentage was previously satisfactory. Iron was given in the form of ferrous sulphate (exsiccatus) suspended in water, in doses of 18 to 20 grains daily for 14 to 21 days.

The haemoglobin level of most recruits improved remarkably during their first three months of army life ; but if iron were also given the improvement was even more striking.

The authors conclude that one of the main causes of anaemia is a low iron reserve in the recruit, which the ordinary army diet is not able to supplement sufficiently. They therefore recommend that all recruits be given 6 grains of ferrous sulphate daily during their training. [Blanket administration of iron to tea-garden coolies has always caused an improvement in their haemoglobin level and general health, and, if the authors' recommendation is put into practice, it will probably be very beneficial to the health of the Indian Army.]

The report includes over fifty tables of haematological data. Its value is considerably enhanced by the systematic statistical criticism.

L. E. Napier.

LURIE, H. I. **Normal Haematological Standards at an Altitude of 5,470 Feet (Witwatersrand, South Africa.)** *Quart. J. Exper. Physiol.* 1945, May, v. 33, No. 2, 91–105, 5 figs. [23 refs.]

The subjects providing the material for this investigation were healthy European residents of the Witwatersrand. They numbered thirty of each sex and their ages ranged from eighteen to forty years.

Venous blood was used for the determination of the absolute indices. The haemoglobin estimations were performed with a Klett-Summerson photo-electric colorimeter which had been carefully calibrated by a variety of methods. The more important results, expressed as mean figures, were as follows. Red cell count, per cmm., males: 5,593,000; females: 4,999,000. Haemoglobin, gm. per 100 cc., males: 17·76; females: 15·33. M.C.V., males: 89·58 $c\mu$; females: 90·42 $c\mu$. M.C.H., males: 31·69 $\gamma\gamma$; females 30·65 $\gamma\gamma$. M.C.H.C., males: 35·47 per cent.; females, 33·82 per cent.

It is noted that these figures show a significant elevation both of the red cell count and of the haemoglobin concentration compared with figures usually accepted as normal at sea level. The rise in the haemoglobin is in conformity with Fitzgerald's law which states that the haemoglobin rises 10 per cent. for every 100 mm. mercury fall in barometric pressure.

Comparing these results with those of previous investigators on the Witwatersrand, the author points out that although the latter show raised red cell counts comparable with his present figures, the haemoglobin readings previously reported were similar to or lower than those considered normal for sea level. He is satisfied that this discrepancy may be entirely explained by the difference in the type of haemoglobinometers used by the earlier workers.

L. J. Davis.

HURTADO, A., MERINO, C. & DELGADO, E. **Influence of Anoxemia on the Hemopoietic Activity.** *Arch. Intern. Med.* 1945, May, v. 75, No. 5, 284–323, 22 charts. [Refs. in footnotes.]

This paper records work performed in Peru, mostly at high altitudes. Very thorough haematological studies, including blood volume and oxygen saturation determinations, were performed on a series of healthy men both at the sea level and at varying altitudes up to 15,860 ft. The subjects studied also included aviators, train crews on Andean railways, Indian natives living at high altitudes, and patients with pneumonokoniosis.

The conclusions may be summarized as follows:—

Exposure to low barometric pressure causes in most cases a polycythaemic response which, at high altitudes, is absolute in type, the total blood volume being elevated as a result of the increased red cell volume. There is also a proportional elevation in the circulating reticulocytes and in the serum bilirubin. It is thought that this latter feature suggests an increased rate of red cell destruction running parallel with the increased production.

Leucopoietic activity is not affected, a temporary leucocytosis, which is occasionally observed on first arrival at a high altitude, being thought to be due to a release or mobilization of stored blood.

Chronic anoxaemia does not modify erythropoietic activity permanently, since, when a native of high altitudes is brought down to the sea level, his blood characteristics eventually resemble those normal in persons living at this level. During the early period of adaptation to normal pressure, however, there frequently occurs an abnormal decrease in the red cells and haemoglobin.

There appears to be a limit for the haemopoietic response to anoxaemia, for, when this is extremely severe, a decrease rather than a further increase is observed in the resulting polycythaemia, which is attributed to an interference

with the formation of haemoglobin. The polycythaemia of high altitudes was compared with polycythaemia observed in individuals living at sea level, and it was concluded that in the latter category, when anoxaemia was due to pulmonary disease, the polycythaemia tended to be of lesser degree than with a corresponding degree of arterial oxygen unsaturation at high altitudes. It is also considered unlikely that the causative mechanism of polycythaemia vera is related to the existence of an anoxic stimulus. *L. J. Davis.*

NEUDA, P. M. & ROSEN, M. S. **Preliminary Report on a Rapid Method for diagnosing Sickle-Cell Disease.** *J. Lab. & Clin. Med.* 1945, May, v. 30, No. 5, 456–8.

This new rapid method for the diagnosis of sickle-cell anaemia and sickle-cell trait is performed as follows.

A cherry-sized quantity of formed human faeces is rubbed up in 5 cc. of normal saline and filtered; 0·1 cc. of the filtrate is transferred to 5 cc. of normal broth and incubated for 24 hours at 37°C. A drop of the resulting "ferment broth" is then gently mixed on a slide with a droplet of the suspected blood, covered with a cover-slip and examined microscopically. In a positive case the appearance of sickling regularly occurs in less than an hour.

The "ferment broth" may be kept at room temperature or in the refrigerator, but it must be renewed every few days, by subculturing into normal broth.

The authors claim not only that the test is invariably positive in cases which show sickling in ordinary sealed wet preparations, but that it is more sensitive than the ordinary methods.

They attribute the mechanism of the test to the presence of an enzyme-like factor in the broth which initiates the process of sickle-cell haemolysis in susceptible cells; and suggest that this factor may be related to the "blood-group ferment" of SCHIFF and BOYD. (Blood Grouping Technic, New York, N.Y., 1942, Interscience Publishers, Inc., p. 182). *L. J. Davis.*

TROWELL, H. C. **Sickle-Cell Anaemia.** *East African Med. J.* 1945, Feb., v. 22, No. 2, 34–45.

Most of the reports of cases of this condition relate to patients of African descent in the U.S.A., relatively few cases having been described in Africa. The present communication comprises a detailed description of a number of cases seen by the author amongst Bantu tribes native of Eastern Central Africa.

The author confirms that the condition is hereditary, being a Mendelian dominant, and manifests itself chiefly in infancy, many patients dying before adult life. Detailed clinical and haematological findings are described in a number of cases and post-mortem findings in two. It is emphasized that the presence of nucleated red cells in the peripheral blood of an African should always suggest sickle-cell anaemia, and that no blood count of an African can be considered complete unless a sealed drop preparation is made and examined for sickle cells. *L. J. Davis.*

VALENTINE, W. N. & NEEL, J. V. **The Artificial Production and Significance of Target Cells. With special reference to their Occurrence in Thalassemia (Cooley's Erythroblastic Anemia).** *Amer. J. Med. Sci.* 1945, June, v. 209, No. 6, 741–52, 3 figs. [13 refs.]

PAPPENHEIMER, A. M., THOMPSON, W. P., PARKER, D. D. & SMITH, Katharine E. **Anaemia associated with Unidentified Erythrocytic Inclusions, after Splenectomy.** *Quart. J. of Med.* (n.s.) 1945, Apr., v. 14, No. 54. 75–100, 17 figs. on 5 pls. [19 refs.]

A careful study is presented of peculiar erythrocytic inclusions that were seen in the peripheral blood of three patients after splenectomy.

The patients, whose ages were 20, 23 and 33 years, were unrelated white Americans living in the Eastern States, with no history of tropical residence. In each case the presenting complaint was severe anaemia of rapid onset accompanied by splenomegaly. In two cases the anaemia was haemolytic in type but was not relieved by splenectomy or other measure and terminated fatally. The autopsy findings are described in detail. In the third case, the anaemia was less severe and also was not significantly affected by removal of the spleen.

In all cases the erythrocytic inclusions were first noted shortly after the splenectomy and were present in all subsequent blood examinations. The affected red cells, which, on an average, constituted 25 per cent. of the total, were seen, in blood films stained with Wright or Giemsa, to contain 1 to 20 or more coccoid or bacillary-shaped inclusion bodies. The bodies were readily distinguishable from the granules of basophilic stippling and from Howell-Jolly bodies. Their staining reactions were positive for iron, but negative with the Gram and Feulgen methods. Attempted culture of the blood in one case was unsuccessful, but cultures in Gieman's medium from the spleen of the same patient yielded a growth, which could be subcultured on to agar, of small pleomorphic organisms morphologically resembling the bodies seen in the peripheral blood, but giving a negative iron reaction and failing to agglutinate with the patient's serum. Inoculations of this culture material into a variety of animals, some of which were splenectomized, and into developing eggs, were all negative. The significance of this organism was thought to be highly doubtful.

The possible relationship of these inclusions to various known blood parasites such as *Bartonella*, *Haemobartonella*, *Eperythrozoon* and *Anaplasma* is discussed at length. It is concluded that no definite proof of their parasitic nature has been obtained, and consideration is given to an alternative interpretation that they are identical with the siderophil granules described by GRÜNEBERG.

[This somewhat lengthy and well illustrated paper should be consulted in the original by all interested, since it is impossible to deal with it adequately in a short abstract. It bears the imprint of careful and competent investigators, and clearly indicates that close attention should be paid to the morphology of the blood cells of patients whose spleens have recently been removed, for if these inclusion bodies are living organisms it would be strange if their topographical distribution were confined to the New York area. Moreover, if, as seems more probable, the inclusion bodies are products of disordered haemoglobin metabolism, the phenomenon is obviously one requiring further investigation.] *L. J. Davis.*

MANN, I. **The Preparation of Dehydrated Liver.** *East African Med. J.* 1945, Jan., v. 22, No. 1, 21–4.

The details are given of a new type of dehydrated liver preparation manufactured in East Africa. The final product is a fine, granular powder of which 1 lb. is derived from 4 lb. of raw liver. To prevent the danger of rancidity and deterioration owing to the presence of fats, the preparation is packed in evacuated and hermetically sealed tins. This substance differs from other liver preparations in that it contains the whole of the liver protein unchanged, and

accordingly, in addition to containing the medicinal properties of liver, it should be valuable as a food. *L. J. Davis.*

Trowell, H. C. **The Treatment of Anaemia in Africans with special reference to a Trial of Dehydrated Liver.** *East African Med. J.* 1945, Jan., v. 22, No. 1, 15–20.

This paper discusses some of the puzzling points regarding the aetiology and nature of nutritional macrocytic anaemia seen by the author in Africans in Uganda. It is noted that, in his experience, the administration of beef, and of food in large amounts, is disappointing therapeutically. Although the patients were found to respond satisfactorily to massive dosage with the cruder liver extracts, the expense of this treatment is considerable. Feeding with whole liver is not always possible because of the difficulty of obtaining it in adequate amounts.

The dehydrated liver preparation described by Mann [above], which was manufactured in Kenya, was found to be of great therapeutic potency in the treatment of these cases. In a daily dosage of 2 oz. it was more active than cooked liver in daily doses of half a pound, and thus appeared to provide an excellent and cheap form of treatment. *L. J. Davis.*

VENOMS AND ANTIVENENES.

Walker, C. W. **Notes on Adder-Bite (England and Wales).** *Brit. Med. J.* 1945, July 7, 13–14, 1 graph.

Three years ago the author published in the *British Medical Journal* a request for information regarding bites by the adder (*Vipera berus*) in Britain. His notes here are based on accounts of 50 persons so bitten. He presents a graph of 30 of them which shows that most cases occur in June (8 cases), next, May and August (5 each), July (4), April and September (3), March and October (1); that is, oftenest in the hot months. Most were on the hand. The symptoms need not be detailed, they were those of viperine poisoning, well known to readers of this *Bulletin*, but comprised, briefly, local pain, haemorrhagic oedema, dilated pupils, faintness, giddiness and varying degrees of collapse with pallor, cyanosis, sweating and loss of consciousness, partial or complete. Recovery was usually complete, but might be slow, with residual pain and stiffness for several weeks. Some patients reported after-effects, but except for one who " shed all his finger- and toe-nails a year after being bitten " [the site is not stated], these had probably little connexion with the original bite. The author states that there have been seven fatal cases in the last half-century, and mentions five of them; the youngest was a child of three years, dying in six hours; another 4½ years (death in 60 hours); the third, a girl of six years in delicate health (36 hours); another, also delicate, aged 11 years (12 hours), and the last an insane adult who lived for 26 hours after being bitten. None of these had been given antivenene. *H. Harold Scott.*

Cilli, V. & Corazzi, G. Studio sugli antigeni del veleno di Echis carinatus eritreo e sui corrispondenti anticorpi. [**On the Antigens of the Venom of *Echis carinatus* in Eritraea and their Corresponding Antibodies.**] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1944, v. 4, No. 4, 641–83. [52 refs.] English summary.

[This is an important and valuable article and contains so much information that the ordinary reader must study it again and again, if he hopes to absorb

it all. In the opinion of the abstracter it would have served its purpose better if the whole had been divided up and the information published in a series of papers, or, on the other hand, the sections might be amplified and the whole issued as a separate monograph. To deal adequately with the article would fill several pages of this *Bulletin* ; hence only the main points can be referred to and those interested must consult the original for details.]

For all the experiments recorded the dried venom kept *in vacuo* and in the dark has been used, diluted with sterile saline for the dosage needed.

First, the toxicity of the venom for laboratory animals was determined by intravenous and subcutaneous injection into rabbits, guineapigs and mice. The results show some peculiar differences [to which, however, the text makes no reference]. For example, 0·01 mgm. per kilo. body-weight intravenously injected will kill rabbits in 10–15 minutes, and 0·02 mgm. in 2–5 minutes. But, for guineapigs, 0·08 mgm. per kilo is needed to cause death in 10 minutes (or eight times the amount needed for rabbits). Subcutaneous injection of 9–10 mgm. per kilo. was needed to cause the death of a rabbit in 12–24 hours, whereas for guineapigs 0·36–0·48 mgm. killed in 27 hours to 5 days, nearly one-thirtieth the dose for rabbits. Mice [weight not stated] required 0·2 mgm. intravenously to cause death in an hour or so and 0·1 mgm. killed in 3–4 hours ; subcutaneously, 1 mgm. killed in 2 hours, 3–4 mgm. in 1½ hours and 1 hour respectively.

Next follows a description of the pathological histology of the different organs—liver, kidneys, adrenals, spleen, lungs, heart and central nervous system. After this come the various determinations included in the title of the article.

First, the coagulating and anti-coagulating activity of the venom, using a modification of the CÉSARI and BOUQUET technique which is described minutely. The outcome of the experiments is that 0·001 mgm. produces complete coagulation of 2 cc. of citrated plasma in 15 minutes. With a dose of 5–10 mgm. anti-coagulative action is revealed, or less if the time of action is prolonged.

The authors next prepared the following substances : (1) Fibrinogen, from citrated horse-plasma ; (2) Serozyme, by Samson Wright's method ; (3) Cytozyme, from Lederle's thromboplastin, and (4) Thrombin, by adding to blood serum 15 volumes of alcohol, collecting the precipitate after several weeks, washing it with alcohol and drying it in a desiccator. It is used as an emulsion in saline. With these, eleven series of experiments (excluding control tests) were carried out, adding the venom in doses ranging from 0,000,005 to 25·0 mgm., to these substances, singly or in combination, and noting the resuls, as regards coagulation. These are given in a table, or rather a series of tablets and discussed. The following conclusions are drawn :—

1. The coagulant action of *Echis carinatus* venom on fibrinogen is, in part, due to a pseudothrombin.
2. Cytozyme does not sensibly affect this.
3. Serozyme increases the action and still more when cytozyme or calcium or both are added.
4. Thrombin increases the coagulant action, in the same degree as the last-named combination.
5. The venom in somewhat greater dosage has an anti-coagulant action due to proteolytic effects on fibrin or fibrinogen.
6. This anti-coagulant action is inhibited in slight degree by cytozyme and calcium, in greater degree by serozyme, whether the other two are present or not.
7. Thrombin weakens the anti-coagulant potency to a degree equivalent to that of adding serozyme.

The authors next proceed to determine the haemolytic action of the venom, using normal horse serum heated to 56°C. for half-an-hour ; four dilutions of the venom, 1 : 1,000, 1 : 10,000, 1 : 100,000, and 1 : 1,000,000, are added to a 5 per cent. suspension of washed red corpuscles of the horse. The venom of *Echis carinatus* is less potent in this respect than that of *V. aspis*, *Cerastes cornutus* or *Naja tripudians*, but equal to, or even greater than, that of the South American snakes, *Sepedon haemachates*, *Bothrops atrox* and *B. nasuta*.

Other experiments were carried out to determine the proteolytic potency of the venom, using fibrin, gelatin, solidified egg-albumin, and solidified serum of the horse. Also the hyperimmunization of horses with anavenin and determination of the anti-coagulant, the anti-haemolytic, the precipitating and the anti-haemorrhagic potencies of the serum so obtained.

Taking these many actions into consideration the authors conclude that since the venom of *Echis carinatus* contains so many constituents—cytolytic, haemorrhagic, neurotoxic, haemolytic, necrosing, liquefactive and coagulant—" the determination of the antitoxic power '*in vivo*' remains the only way of measuring the true protective value of an antivenene." *H. Harold Scott.*

ROY, A. C. **Lecithin and Venom Haemolysis.** [Correspondence.] *Nature.* 1945, June 9, 696–7.

KLEINMAN, A., PAGE, R. C. & PREISLER, P. W. **Prothrombin Studies using Russell's Viper Venom. VII. Effect of Prothrombin Clotting Time of the Concentrations of Calcium and other Salts.** *J. Lab. & Clin. Med.* 1945, May, v. 30, No. 5, 448–50.

GRASSET, E. **Anavenoms and their Use in the Preparation of Antivenomous Sera. Polyvalent Anti-*Bitis arietans-Naia flava* Serum and Specific Antivenenes against African Viperine and Colubrine Venoms.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, July, v. 38, No. 6, 463–88. [15 refs.]

The author and his fellow-workers have shown on previous occasions the value of anavenoms—a term proposed by RAMON in 1925 for venoms detoxicated by addition of formol—in obtaining in a comparatively short period highly potent antivenenes. The method has been in use for more than a decade at the South African Institute for Medical Research.

Several factors have to be taken into account in producing anavenoms, such as the venom concentration, the solvent, the concentration of formol, the *p*H and buffer, the temperature and the period of detoxication. In the present paper an account is given of the details of the procedure and technique. First is considered the question of the concentration of venom to be used in detoxication and the amount of formol sufficient to detoxicate while interfering as little as possible with its antigenic properties. This was done with *Bitis arietans* (the common puff-adder of South Africa), *B. caudatus*, *B. cornutus*, *B. gabonica* and *B. nasicornis* ; *Causus rhombeatus*, *Naja flava* and *Sepedon haemachetes*, and others, and at the Institute there has been prepared a polyvalent antivenene against the African snakes of the *Naja*, *Sepedon* and *Bitis* genera. The details are of much interest and are so clearly set out that any worker in this field can follow and repeat the instructions. Interested workers must consult the original ; to reproduce them here would occupy too much space.

The author next considers the rôle of buffer and the *p*H in anavenom preparation, showing that the main effect is on the physical condition of the product. For obtaining antivenenes, horses are injected with mixed anavenoms in graded dosage ; a week after the last injection a sample of the blood is taken

for an *in vitro* test of the titre, and if this is satisfactory the horse is bled (10 litres) and, two days later, another 10 litres are removed. After 4–6 weeks' rest the animals are re-immunized by three subcutaneous injections of the anavenoms at weekly intervals and, as before, the serum is tested and a week later the horses are again bled. When the response begins to fall off and supplementary injections do not restore it, the animal is discarded. [See also this *Bulletin*, 1934, v. 31, 103; 1936, v. 33, 382, 383; 1937, v. 34, 722, 723; 1938, v. 35, 522; 1940, v. 37, 514.] *H. Harold Scott.*

AHUJA, M. L. & BROOKS, A. G. *In vitro* **Test for Assay of Potency of Cobra Antivenene.** *Indian J. Med. Res.* 1944, Oct., v. 32, No. 2, 227–31.

Snake venoms having a complex antigenic structure, there is no international standard of the potency of antivenenes. The results of tests on pigeons *in vivo* are very varied even with birds of the same weight and with the same venoms and antivenenes, so that, to obtain an average, many pigeons may have to be sacrificed. Hence the need for a better and more reliable method.

The observation has been made that washed red corpuscles of certain animals, the guineapig, for example, are haemolysed by cobra and daboia venoms, but that this haemolysis is inhibited if antivenene is present. The authors have, therefore, devised an *in vitro* method of estimating the antihaemolytic titre of cobra antivenene and this was found to be so closely approximate to the anti-neurotoxic titre in pigeons that it is suggested as a substitute for the latter. The procedure is on standard lines. The haemolytic effect on guineapig cells is estimated by adding diluted venom in graded doses to 3 per cent. suspension of the cells. Then another series is set up in which the venom and the serum under test, made up to a fixed amount, are shaken and then incubated at 37°C. for an hour, after which a fixed quantity of the red cells in normal saline is added, the whole shaken to procure good mixing, and allowed to stand at room temperature for 18 hours, when the result regarding haemolysis is noted. An example is given in these words:—

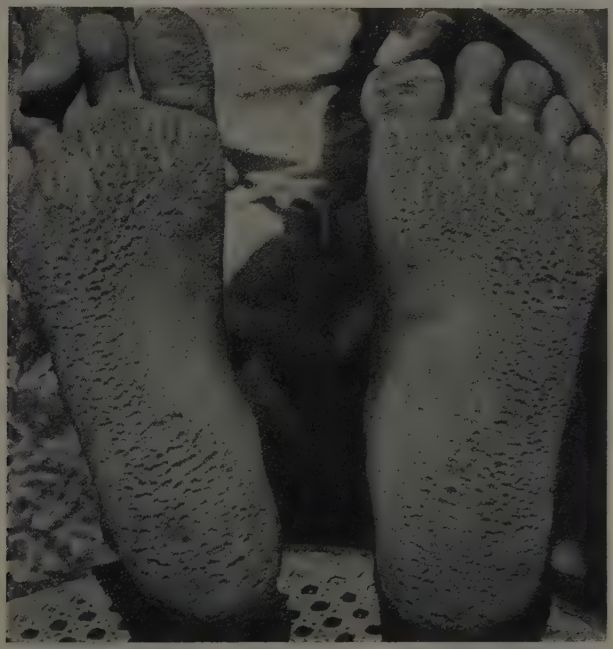
"The sample of venom used in the *in vitro* test had a minimum haemolytic dose of 0·03 mg. for 1 cc. of 3 per cent. guinea-pig cells, and that used for the *in vivo* test had a minimum lethal dose of from 0·3 mg. to 0·4 mg. for pigeons of standard weight. The anti-haemolytic potency of the various sera tested varied and according to the results obtained they have been arranged in three different categories . . . . In group A haemolysis—partial or complete—occurs with 0·4 mg. or less of venom. In group C partial or no haemolysis occurs with 0·6 mg. of venom, and in the intermediate group B partial or complete haemolysis occurs with 0·5 mg."

The close correlation between the *in vitro* haemolysis and the *in vivo* tests with pigeons is shown by the fact that group B serum, in which 0·4–0·5 mgm. of venom is neutralized by 1 cc. of the antivenene, may or may not pass the *in vivo* test, but group C serum (0·5 mgm. venom being neutralized) does pass the test. Hence it is concluded as generally true—there are occasional anomalies—that "if the anti-haemolytic titre of a serum is less than 0·4 mgm. per cc., it is not up to standard titre; if it is over 0·5 mg. per cc. it is up to titre; and if it is between 0·4 mg. and 0·5 mg. per cc. it is on the border line and may or may not be up to titre." *H. Harold Scott.*

DERMATOLOGY AND FUNGOUS DISEASES.

FASAL, P. **Cutaneous Diseases in the Tropics : a Clinical Study based on Observations in Malaya.** *Arch. Dermat. & Syph.* 1945, Mar., v. 51, No. 3, 163–71, 7 figs.

This is entitled a clinical study, but is little more than a list of cutaneous conditions met with during three years in Malaya. More than 70 diseases receive mention in these few pages. The author includes under " cutaneous diseases " such things as new growths, fibroma, lipoma, angular stomatitis



Keratoma plantare sulcatum on a Tamil man.
[Reproduced from the *Archives of Dermatology and Syphilology.*]

from irritating fruits, also the rash of dengue, tsutsugamushi fever, lymphogranuloma inguinale, Madura foot, elephantiasis and others.

The author divides the diseases into three large groups : (1) Those due to external causes, among which he mentions sunburn, sudaminal rashes, prickly heat, dhobie itch and various forms of dermatitis venenata as rengas and upas tree (*Antiaris toxicaria*) rashes, necrosis from injuries inflicted by catfish and the sting-ray, scorpion stings, etc., cheilitis from mango, papaya and other fruits. Also keratoma plantare sulcatum, probably due to walking barefoot on hot and moist soil. A good example of this is shown in a photograph. (2) A second group comprises conditions associated with nutritional deficiencies, such as ichthyosis, " crazy pavement skin," pellagra and angular stomatitis. (3) Thirdly, cases

arising from infection by animal and plant organisms. Among these the author places the exanthemata—dengue, varicella, herpes zoster, molluscum contagiosum, Japanese River fever, venereal diseases; also impetigo and furunculosis, tuberculosis and leprosy, pityriasis versicolor, eczema marginatum and tinea imbricata, tropical ulcer and elephantiasis. Lastly, mention is made of urticaria, purpura, erythema occurring in malaria patients taking quinine, also of psoriasis and lichen planus. These all receive passing mention, but rarely more than a few words each. Obviously hardly more could be said when so many conditions are referred to in so small a space. *H. Harold Scott.*

Fernández, J. M. M., Vaccaro, A., Serial, A. & Carboni, E. Discromias de probable etiología espiroquetósica (Mal de Pinto ?). [**Dyschromia associated with Spirochaetosis. Pinta ?**] *Rev. Argentina Dermatosifilologia.* 1945, Mar., v. 29, No. 1, 1–10, 6 figs.

Notes are given of five cases of a peculiar symmetrically distributed achromia in patients whose ages ranged between 19 and 54 years. Face, trunk and limbs were affected. The Wassermann reaction was negative (except in one

Case of symmetrically distributed achromia.
[Reproduced from the *Revista Argentina de Dermatosifilologia.*]

where it was doubtful and the patient gave a history of contracting syphilis years before). Spirochaetes were to be seen in fluid obtained at the edge of the patches. The authors are of opinion that the condition is not something new, but merely a variety of mal del pinto. *H. Harold Scott.*

Obermayer, M. E. & Frost, K. **Some Phases of Vitamin Therapy in Dermatology.** *Arch. Dermat. & Syph.* 1945, May, v. 51, No. 5, 309–12. [21 refs.]

The authors would divide a varied group of dermatological conditions into two groups—(*a*) in which an aetiological relationship has been established

between the condition and a specific vitamin, and (*b*) " dermatoses in which a true vitamin deficiency is either debatable or undemonstrable but for which vitamin therapy appears to be of benefit."

They appear to agree with the observations of others that a high intake of vitamins A, C, D and the B complex aid in the control of the allergic state, or the allergic factor in a variety of dermatological conditions, their action possibly being due to the " antidermatitis and hypochlorhydria-preventing " fractions of the B complex. It is suggested as a warranted fact that the ingestion of thiamin will render a sensitive subject tolerant to insect bites or even repellent to the insects themselves.

In regard to vitamin A it is stated " large doses seem to affect a large number of dermatological diseases by their influence on the integrity and resistance of epidermal and epithelial surfaces but the mechanism of the effect of vitamin A on the epithelial tissues has not been explained " ; the skin contains no vitamin A and " carotenoid levels of the blood plasma of patients with a number of diverse cutaneous diseases have not revealed characteristic deviations."

Attention is focussed on those dermatoses characterized by excessive keratinization, either more or less diffuse, or limited to the follicular system. Abnormal callus formation of the skin and hyperkeratotic chronic simple lichen are stated to respond, and among the second group lichen pilaris, keratosis follicularis, pityriasis rubra pilaris and acne vulgaris are represented as having been cured.

These conditions are quite apart from the follicular hyperkeratosis which the authors admit, as many others have done, as a specific sign of vitamin A deficiency.

[Doubtless vitamins play a part in maintaining the nutrition of the skin, but when it is necessary to give from 20 to 100 times the normal daily intake over a period of 6 to 18 months to effect a change in the above-mentioned conditions, one begins to wonder whether any effect produced is of the nature of a specific response to such treatment. Recently, doubt has been cast upon the belief that follicular hyperkeratosis is a sign of vitamin A deficiency. The wise man will continue to experiment but reserve his interpretation of results till later.] *H. S. Stannus.*

SYMMERS, D. **Experimental Reproduction of Maduromycotic Lesions in Rabbits.** *Arch. Pathology.* 1945, June, v. 39, No. 6, 358–63, 5 figs.

" Phialophora jeanselmei when injected subcutaneously into rabbits produces solitary non-ulcerative nodules which histologically are specific and are closely comparable to the nodules in that form of maduromycosis in man which is caused by the same fungus."

EMMONS, C. W. *Phialophora jeanselmei* **comb. n. from Mycetoma of the Hand.** *Arch. Pathology.* 1945, June, v. 39, No. 6, 364–8, 2 figs. [12 refs.]

" The mycologic characteristics of a fungus isolated from mycetoma of the hand are given. The condition developed after an injury in which splinters from a wooden floor pierced the skin. The fungus resembles Phialophora, which is known to occur on wood. It is specifically identified with Torula jeanselmei Langeron which was isolated from mycetoma of the foot. This species is transferred to Phialophora, the name becoming Phialophora jeanselmei comb. n."

LEVY, B. & BLACK-SCHAFFER, B. **Studies in Experimental Systemic Mycosis. I. Systemic Chromomycosis (Chromoblastomycosis) in Mice : Preliminary Study.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 117–27, 11 figs.

The lesion of chromomycosis is cutaneous-subcutaneous, and metastatic spread of the infection to the deeper tissues is so rare that only two instances

are recorded in the literature. To investigate the possibility of infection of the deeper tissues, Levy and Black-Schaffer inoculated five white mice by the intravenous route and five others by the intraperitoneal route with a fresh culture of the causative fungus *Hormodendron pedrosoi*, ground up and suspended in isotonic saline. The mice were sacrificed and examined at intervals between the 7th and 27th days following inoculation. Intraperitoneal inoculation caused only a local lesion with, in one case, slight extension of the infection into the stomach wall. Intravenous inoculation, as would be expected, led to widespread distribution of the fungal elements, with miliary granulomatous lesions mainly in the lungs—the first capillary area encountered—and in lesser degree in the kidneys. The cytological structure of the granulomata was of the kind associated with chromomycosis and other mycoses, and was not merely a foreign body reaction. In many of the granulomata there was evidence of survival and growth of the fungus and, in one case, small satellite lesions suggested an extension of the infection. The time allowed for survival of the mice after inoculation was too short to determine that a progressive infection had been established ; the experiments will therefore be repeated with longer time intervals. *J. T. Duncan*

Rodhain, J. Documents complémentaires au sujet des teignes au Mayumbe. [**Additional Information on the Ringworms of Mayumbe.**] *Ann. Soc. Belge de Méd. Trop.* 1943, Sept.–Dec., v. 23, Nos. 3–4, 257–8, 5 figs. on 2 pls.

TROPICAL ULCER.

Walker-Taylor, P. N. **Treatment of Tropical Ulcer.** *Lancet.* 1945, July 14, 40–42.

" Tropical ulcer is a straightforward subject, and difficulties are created only by a wrong conception of its nature."

" The treatment is elementary . . . . This is attained by two rational steps : (1) Arranging conditions so that fresh granulations will fill the tissue gap . . . . (2) Arranging conditions for re-epithelialisation of the surface before fibrosis has been allowed to develop."

The author points out that the above refers to the treatment of the " de novo tropical ulcer as it is first seen."

(1) The first step is taken by insisting on continuous stay in bed, and for West African natives the leg must be tied to a fixed appliance to keep the patient in bed. This is all that need be done, but warm moist compresses and penicillin or sulphonamide powder locally are useful aids and, since dressings must not be allowed to become dry, soft paraffin is the best application.

(2) The ulcer being now clean and filled with granulations, skin grafting should be done without delay ; the author prefers " pinch grafts."

When a toenail is involved, sufficient drainage must be provided by cutting away *dead* cuticle and *dead* nail ; then the cavity is disinfected and packed with gauze soaked with 10 per cent. silver nitrate solution, to prevent pus from passing into it from the surrounding part of the ulcer.

The author gives two tables for comparison ; the first analyses 210 cases of tropical ulcer admitted to hospital and treated in various ways from January 1st to May 31st, 1944, and the second analyses 47 cases admitted to the author's wards from July 10th to October 10th and treated in the way described above. In the latter group the average time of healing (17·8 days) was less than half that (37·2 days) in the former.

In a letter to the *Lancet*, 1945, July 28, 124, MILLS points out that acute ulcers spread very rapidly and that the application of pure carbolic is the best means of preventing this and of securing a granulating surface for pinch grafts.
J. F. Corson.

SORICELLI, F. Contributo radiologico alla conoscenza di alcune lesioni osteo-periostee nell'ulcera tropicale. [**Radiological Investigation of Osteo-periostitis in Tropical Ulcer.**] *Boll. Soc. Ital. di Med. e Igiene Trop.* (Sez. Eritrea). 1944, v. 4, No. 3, 487–96. English summary (6 lines).

MISCELLANEOUS DISEASES.

BINNS, R. T. **A Study of Diseases in Australian Natives in the Northern Territory.** *Med. J. Australia.* 1945, Apr. 28, v. 1, No. 17, 421–6.

These observations were made during the occupation of the Northern Territory of Australia by the army. A native hospital was built near the Australian general hospital and was situated on the bank of the Katherine River [apparently about 14° 30′S. × 132°E.]. Patients came from all parts of the northern districts of the territory and various surrounding settlements were visited and medically surveyed. From September 1943 to October 1944, about 400 natives were treated at the hospital and about 250 were examined at the settlements. Surgical cases and ophthalmic cases are not included in this report but the author mentions that " a large majority of natives were found to be suffering from trachoma . . . . "

The diseases which affected natives more than white people were yaws, ankylostomiasis, granuloma venereum [ulcerating granuloma of the pudenda], and leprosy. The Kline test of the blood was positive in 193 (48 per cent.) and 81 had clinical signs of yaws. Hookworm ova were found in 12 per cent. of natives admitted to hospital ; usually the infestation produced no symptoms, but in a few cases severe anaemia was caused. There were 20 cases—10 in each sex—of granuloma venereum, and 12 cases of leprosy.

The disease common to both natives and white people included pneumonia (32), pulmonary tuberculosis (21), acute rheumatism (5), meningitis (1), mumps (24), benign tertian malaria (20), Flexner type of dysentery (4), amoebic dysentery (2), and gonorrhoea (11). The course of tuberculosis in natives was similar to that in Europeans, and the frequency of the occurrence of fibrosis and calcification indicated the existence of some natural resistance ; the authors think that the problem of control is not so hopeless as has sometimes been taught.
J. F. Corson.

DUBOIS, A. La pathologie du Congolais. [**Diseases of the Inhabitants of the Belgian Congo.**] *Ann. Soc. Belge de Méd. Trop.* 1943, June 30, v. 23, No. 2, 69–89. [31 refs.] ; 1944, June 30 & Sept. 30, v. 24, Nos. 1–2 & 3, 13–28. [54 refs.] ; 79–100 [61 refs.].

In these papers the author gives a general survey of the prevalence of various pathological conditions among Africans of the Belgian Congo. The account was largely written from memory in the absence of records ; some information was received from colleagues. Many references are made to work in other parts of tropical Africa and the Far East.

Chronic valvular disease of the heart is not rare ; acute rheumatism being

very rare, the causes are not known but it is thought that syphilis is one. Aneurysm of the aorta and large arteries and endarteritis obliterans are also not rare.

Bronchopneumonia is commoner than lobar pneumonia ; Loeffler's syndrome has recently been observed.

Among diseases of very rare occurrence are peptic ulcer, appendicitis and calculus (biliary, renal and vesical). Cirrhosis of the liver, apart from schistosomiasis, is probably not common but the author has no figures. Goitre is common in some places ; exophthalmic goitre is unknown.

Haematology has been studied by VAN DEN BERGHE [this *Bulletin*, 1943, v. 40, 262]. RODHAIN (personal communication) observed 2 cases of Hodgkin's disease.

Among diseases of the nervous system, epilepsy is fairly common in certain areas. GREGOIRE (unpublished), at Léopoldville, noted 24 cases of cerebral syphilis and 8 of general paralysis among 155 insane natives.

Skin diseases were investigated by DUBOIS and BRUYNSEELS [this *Bulletin*, 1943, v. 40, 176]. *J. F. Corson.*

SUÁREZ, R. M. **The Incidence of Heart Disease in Puerto Rico. Statistical Analysis of 1,081 Cases.** *Amer. Heart J.* 1945, Mar., v. 29, No. 3, 339–47, 1 fig. [19 refs.]

All of those with whom this analysis deals were native Porto Ricans ; their ages ranged between 8 and 83 years ; only 10 per cent. were negroes ; one-third were females, two-thirds males. Examinations were thorough, with electrocardiograms, cardiac measurements, vital capacity, venous pressures, and the Wassermann, Kahn or Kline tests. In the 27 years since 1915, heart disease as a cause of death had risen from seventh to fourth place, being surpassed only by intestinal conditions, tuberculosis and pneumonia. Among 1,259 consecutive autopsies 128 (10 per cent.) were found to have cardiovascular disease as the cause of death, and of these 38 (30 per cent.) were syphilitic, 26 (20 per cent.) rheumatic, and 22 (17 per cent.) arteriosclerotic. Just over half the syphilitics (20 of the 38) showed aortic aneurysm.

In 1942 heart disease was the cause of death of 2,177, or 111·9 per 100,000 population, the urban rate being more than double that of the rural (170·2 to 81). Rheumatic fever is generally believed to be rare in the tropics ; this applies to joint symptoms and clinical manifestations, but rheumatic heart disease is far from uncommon.

Among the 1,081 analysed there were 15 per cent. (163) cases of coronary disease and 40 per cent. of those with arteriosclerotic heart disease presented evidence of myocardial infarction.

In Porto Rico the percentage incidence of the chief types of heart disease is : arteriosclerosis 39·9, hypertension 22·8, rheumatic fever 17·4, syphilis 6·1. The author compares these Porto Rico figures with those of Mexico, Virginia and Louisiana in a table, from which it is seen that Porto Rico is highest in arteriosclerosis, but lowest in syphilis. *H. Harold Scott.*

APLEY, J. & GRANT, G. H. **Tropical Eosinophilia as seen in England.** *Lancet.* 1945, June 30, 812–13. [19 refs.]

In September 1944 the authors reported on a case of tropical eosinophilia in an Englishman home from India. They drew up a very useful table contrasting the so-called Loeffler's syndrome with typical " tropical eosinophilia " and then demonstrated that none of the differences thus set down was really valid, but represented extremes of one condition [this *Bulletin*, 1944, v. 41, 1065].

The authors now record four more cases, three very similar to the first, the fourth showing certain differences, among 113 consecutive patients invalided home from the East on account of pulmonary conditions, chiefly asthmatic. A table summarizes the chief features of all five cases (the original and the four new ones), showing that four of the patients had been in India [the cases are oftenest reported from the Bengal coast] and one in China after a brief stay in Ceylon ; all complained of cough, bronchitic or asthmatic symptoms, worse at night, with loss of weight. Eosinophilia ranged between 7 and 32 per cent. before treatment with arsenicals in England, reduced to 1–5 per cent. two weeks after a course of NAB.

In view of the various conditions which have been assigned [largely on account of their concomitant presence] as causes of the syndrome, numerous investigations were carried out on all five patients, notably repeated X-ray examinations of the chest, blood counts, faecal examinations for helminths or their ova, sputa, and blood for filariasis.

Treatment consisted of arsenic injections ; three intravenously of 0·3 gm. of neoarsphenamine, followed by three more of 0·45 gm., also intravenously, with ascorbic acid and calcium gluconate, at 3–4 day intervals. During the course the eosinophilia increases, but it falls within a fortnight afterwards, either rapidly or more slowly over a period of several weeks.

The authors conclude that these are allergic manifestations, the common result of, perhaps, several kinds of allergen, introduced, it may be, by mites where such have been found (as by CARTER *et al.*, this *Bulletin*, 1945, v. 42, 73). The fifth case differed from the others, notably in the characters of the cells seen in smears from sternal puncture, and the authors think that this patient was not suffering from the same disease as the others [or it may be that the allergen was not the same]. A remarkable difference from the cases generally recorded is the absence of splenomegaly from all five. [Nothing is said of any lymph-gland enlargement, as reported by VAN DER SAR and HARTZ (below), and others. The more this condition is studied the more complicated it becomes, and the difficulties, instead of being cleared up, seem to increase. There is here an excellent field for research.] *H. Harold Scott.*

VAN DER SAR, A. & HARTZ, H. **The Syndrome, Tropical Eosinophilia and Microfilaria.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 83–96, 8 figs. [25 refs.]

The author starts his paper with a good survey of the literature of the last quarter of a century dealing with Loeffler's syndrome, eosinophil lung, tropical eosinophilia. He then relates four cases, three of them under his own observation, with leucocytosis, eosinophilia (relative and absolute), nocturnal asthma with splenomegaly and enlarged lymph glands. The fourth case was that of a boy of 7 years killed in a motor accident ; in life he had recently suffered from asthma and anaemia. In the first three, improvement and final recovery followed the administration of arsenicals.

The important point of this contribution is that sections of the glands in the first and of the spleen in the last case, showed the presence of microfilariae with local eosinophilia (eosinophilic abscesses). In the other two the pathological histology was similar, but no worms were seen (but, in one at least, serial sections were not made). The only known Filaria in Curaçao is *W. bancrofti*.

The authors maintain, therefore, that there seems to be a relationship between filariasis and tropical eosinophilia, but whether all cases of this syndrome are so related can only be determined after many more have been

examined, by biopsy of enlarged glands, for example, in the various places where these cases have been reported. Photomicrographs showing the pathological histology are well reproduced. *H. Harold Scott.*

HIRST, W. R. & MCCANN, W. J. **Tropical Eosinophilia ; Report of a Case.** *U.S. Nav. Med. Bull.* 1945, June, v. 44, No. 6, 1277–81, 1 fig.

The main interest of this case lies in the fact that the patient, though he had served in the South Pacific and other warm climates, had never been in India. His symptoms were typical: feverishness, malaise, headache, asthmatic attacks, especially at night, with leucocytosis to about twice normal and an eosinophilia to 82 per cent. His symptoms had begun two years prior to his coming under the author's care, when he was in Samoa. None of the ordinary causes of eosinophilia was present (except the asthma) ; there were no indications of helminthic infestation, the Kahn reaction was negative. He was given neoarsphenamine, starting with 0·15 gm., then at four-day intervals 0·3, 0·45, 0·6 and 0·6 gm. The response was dramatic. At first there was a fall of leucocytes, followed, as usual, by a rise, though of the eosinophiles to a less degree, and then a reduction of the total leucocytes and of the eosinophile percentage. In three weeks the total had dropped to normal, but the eosinophiles were still 20–25 per cent. ; later they fell to 4–16 per cent. and the patient " never felt better."

Among the authors' conclusions are: (1) That, since the symptoms had resisted all the usual forms of treatment for almost two years, they might very likely have persisted indefinitely, had not the specific treatment with arsenic been started. (2) That the ready response to arsenic points to a spirochaete or a protozoon as the cause. (3) That either the disease is endemic in the South Pacific, or infection is transmissible from man to man, for the patient had been in contact with East Indians at Panama, though he had never himself, as already stated, been in India. *H. Harold Scott.*

CHAUDHURI, R. N. & RAI CHAUDHURI, M. N. **A Case of Tropical Eosinophilia developing Agranulocytic Angina during Arsenical Therapy.** *Indian Med. Gaz.* 1945, Mar., v. 80, No. 3, 151–3, 1 pl. & 1 chart.

GENERAL PROTOZOOLOGY.

KIRBY, H. **Some Observations on Cytology and Morphogenesis in Flagellate Protozoa.** *J. Morphology.* 1944, Nov., v. 75, No. 3, 361–421, 1 text fig. & 8 pls. (67 figs.). [165 refs.]

Certain flagellates, apart from the evident external structures such as flagella and undulating membranes, possess complicated internal structures or organelles, of which the blepharoplasts, kinetoplasts, parabasals, costa and axostyles are examples. When multiplication by binary fission occurs, some of these divide, one product passing to each daughter individual ; others are completely absorbed, new organelles being developed for each daughter flagellate. In the paper considered here the author discusses the behaviour of a number of flagellates in these respects, making special reference to some of the larger forms found in termites, certain trichomonads and *Trypanosoma brucei*. The paper, which is well illustrated, should be read by those interested in the morphology of the group of Protozoa. *C. M. Wenyon.*

MANWELL, R. D., COULSTON, F., BINCKLEY, Ellen C. & JONES, Virginia P. **Mammalian and Avian** *Toxoplasma*. *J. Infect. Dis.* 1945, Jan.–Feb., v. 76, No. 1, 1–14, 8 figs. on 1 pl. [20 refs.]

This is an interesting review of knowledge regarding three types of parasite which have been referred to as toxoplasma, combined with an account of certain original observations and experiments. In the first place a study was made of a mammalian strain of human origin. This was inoculated to four species of mammals and six species of birds. Attempts to infect frogs failed entirely. Infections were produced by intracerebral and intraperitoneal inoculations as well as by feeding on infected tissues. It would seem that all warm-blooded animals are susceptible, there being amongst them a complete lack of host-specificity. The type of infection varied, being sometimes acute and at other times chronic. After intracerebral inoculation the infection and symptoms were chiefly cerebral, while after intraperitoneal inoculation they were mostly abdominal, though in both cases generalized infection occurred in which different organs and many types of cell became involved. As regards the natural method of transmission there is little information. Healthy animals failed to become infected when kept in contact with those infected, though intestinal washings of infected animals produced infection by the mouth. Infected mice pass the infection to offspring *in utero*. The parasite is easily killed by drying and disinfectants. It will survive in the ice box for not longer than 48 hours but will withstand complete freezing for a short time. The only method of cultivation which was successful was the chick-embryo method within the egg.

The second type of toxoplasma has been found in small birds, where it is commonly seen in lymphocytes, lying in a notch in the nucleus. It is completely host-specific, all attempts to subinoculate having failed. Birds infected with it are in no way protected against the mammalian toxoplasma. Furthermore, it can be distinguished morphologically. The authors conjecture that it is not a toxoplasma but probably represents straying merozoites of a coccidium. The third toxoplasma, the " X-bodies," is also of avian origin and is found commonly in the lungs of canaries and possibly other small birds. Like the second, it is not inoculable to other hosts, and fails to give protection against the mammalian form. It also may represent merozoites of a coccidium.

The general result of the enquiry is that the mammalian form alone belongs to the genus *Toxoplasma* and that all strains isolated from mammals will be found to belong to the original species *T. gondii* of NICOLLE and MANCEAUX, though various authors have given specific names according to the hosts in which the parasite has been found. *C. M. Wenyon.*

GENERAL ENTOMOLOGY.

BUXTON, P. A. **The Use of the New Insecticide DDT in relation to the Problems of Tropical Medicine.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, May, v. 38, No. 5, 367–93. [32 refs.] Discussion 393–400. [SCOTT, H. (President) ; MACDONALD, G. ; BUSVINE, J. R. ; MELLANBY, K. ; SINTON, J. A. ; WENYON, C. M. ; BUXTON, P. A. (in reply)].

The ideal insecticide, in addition to being highly toxic to insects, should be safe to man and mammals, and stable under natural conditions ; it should not stain, have an offensive smell or harmful effect on fabrics, metals, etc. ; it should be easily manufactured at low cost, and be adaptable to many methods or purposes. DDT, dichlor-diphenyl-trichlorethane, or alpha alpha-bis

(p-chlorphenyl) beta beta beta-trichlorethane fulfils these requirements more nearly than any other substance. It is an exceedingly non-volatile, white crystalline powder, with a faint pleasant smell. It melts at 108°C.; the molecular weight is 354·5, the density 1·6 gramme per ml.; and it dissolves in most organic solvents, though the solubility in water is very low. In mineral oils it tends to be more soluble in the less highly refined specimens, the solubility in kerosene being 4 per cent., that in various fuel oils 8 to 10 per cent. Commercial samples are usually mixed with other substances, mostly isomers which are only slightly insecticidal, and have a purity of 60 to 70 per cent.

Solid DDT ground with a mineral diluent is harmless when applied to the skin, and does not retard the healing of cuts. When applied to the skin in solution, DDT is absorbed, and symptoms occur in experimental animals after daily application of 150–1,200 mgm. per kgm. Dimethyl and dibutyl phthallates do not increase the absorption of DDT in comparison with other solvents. There are no records of dermatitis after DDT, and sensitization is uncommon. It is not harmful to the eye, including the conjunctiva, and ointments up to 5 per cent. have been put on the conjunctiva without ill-effect.

When experimental animals and men are exposed to concentrated mists of DDT solution, and dusts of the powder they do not suffer ill effects, and no danger is to be expected following inhalation of sprays or dust during insecticidal work. However, precautions should be taken to prevent the heavy contamination of food.

When single doses of oil solutions are given to experimental animals by the mouth, the median lethal dose varies from 150 to 600 mgm. per kgm., and continuous dosage with 50 mgm. per kgm. per day is fatal to rabbits. Symptoms are slow in onset, initiated by abnormal excitability and tremors, going on to flaccid paralysis and death. [For an account of symptoms in man see WIGGLESWORTH, *Bulletin of Hygiene*, 1945, v. 20, 411]. At post-mortem examination in animals exposed to toxic doses of DDT minor nervous changes are seen, with large areas of necrosis in the liver. The author concludes that DDT used as an insecticide is quite safe.

DDT is more general and less specific in its action on arthropods than most insecticides, but the lethal dose for different insects varies greatly, that for *Rhodnius*, for instance, being 10,000 times that for *Aëdes*. It acts as a contact poison, and has a very slow effect, death being preceded by inco-ordinated and violent movements. It is not repellent to insects and is not a fungicide.

Against flies and mosquitoes it may be used as a spray, most such sprays now consisting of DDT to kill the insect with some pyrethrum to ensure quick knockdown, or as a film on surfaces. Films for which a dose of 100 mgm. per sq. ft. should be aimed at, hold the number of mosquitoes in treated rooms down to a very low figure for 2 or 3 months after a single application. Much entomological work is necessary on this subject, as the probability of killing is influenced by the habits of the mosquito, and the type of place in which it rests. A particularly important point is that the use of such films may solve the problem of transport of insects by aircraft. Field tests of the dry powder as a larvicide have been disappointing, despite encouraging laboratory results, but 5 per cent. oil solutions have proved effective in doses of 1 to 2 quarts per acre, and under experimental conditions in doses as low as 0·1 cc. per square yard [0·85 pints per acre], which gives some residual effect needing further enquiry, as does the use of colloidal solutions. Distribution of oil solutions by aircraft not only kills larvae, but also many adult mosquitoes contaminated either directly or by picking up DDT from surfaces at night.

Adult house flies may also be killed by sprays or films, the recommended strength of sprays being 0·3 or 0·5 per cent., with 0·05 or 0·03 per cent. pyrethrins, respectively. Films of 25 mgm. per square foot are effective, though the

dose varies with the nature of the wall surface, painted surfaces needing more than plain wood, and glass surfaces very minute quantities. It has also been shown that many other muscids, including *Calliphora, Lucilia, Chrysomyia, Stomoxys* and *Glossina* are very susceptible to DDT in the form of a residual film, and very promising results in their control have been obtained. DDT has also been used in emulsion against the larvae of the housefly with success.

As an insecticide against lice, DDT is very valuable, and a 10 per cent. mixture with talc is now commonly used ; it remains effective for 2 or 3 weeks, and may kill lice after that, assuming that the subject does not wash his garments. For men in winter clothes, 1½ ounces per treatment suffices. It was used in the control of typhus in Naples early in 1944 on a very large scale, and this has been described as " the only completely proven victory which can as yet be ascribed on DDT's battle honours." An even more effective method is by impregnating garments with 1 to 2 per cent. of DDT from solutions or emulsions.

DDT has also been used against head lice as a dust, or in emulsions, in which form 0·2 gm. completely proofs the head for a week.

DDT is without doubt the most effective material known for bug control. Experimentally, films of about 0·2 mgm. per square cm. (180 mgm. per square foot) remained lethal for from one to six months. The type of surface and the method of application affect results and dosage. In practical trials, it has been found that a dose of about 100 mgm. per square foot kills any bugs brought in within three months.

Cockroaches are relatively resistant to DDT. A five per cent. powder is very effective against fleas. Trombiculid mites die after running on impregnated garments, but as the effect is slow and wears out with washing, this method is of little value against the vector of scrub typhus. There has been recorded, however, a marked reduction in mites on ground dusted with 30 lb. of 2 per cent. DDT per acre.

[The author refers to the non-appearance so far of any accurate account of the use of DDT in the Naples typhus epidemic of 1943–44. A statement giving the weekly incidence of cases, the dates on which DDT was used, and the scale on which it was used, must be awaited before DDT can be given credit for ending the epidemic.] *G. Macdonald.*

(i) ROARK, R. C. **A List of Publications on 2, 2-bis (Parachlorophenyl)-1, 1, 1-Trichloroethane (called DDT) from 1874 to April 30, 1944, Inclusive.** *U.S. Bureau Entom. & Plant Quarantine.* 1944, June, 12 pp. [Processed.]

(ii) —— & MCINDOO, N. E. **A Digest of the Literature on DDT through April 30, 1944.** *U.S. Bureau Entom. & Plant Quarantine.* 1944, Dec. E–631. 53 pp. [Processed.]

(iii) ——. **A Second List of Publications on DDT.** *U.S. Bureau Entom. & Plant Quarantine.* 1945, May, E–660, 27 pp. [Processed.]
[Summary appears also in *Bulletin of Hygiene.*]

In June 1944 the U.S. Bureau of Entomology and Plant Quarantine issued a list compiled by ROARK of 174 articles on DDT published from the time of its original synthesis in 1874 up to April 30, 1944. In December 1944 a digest (E-631) by ROARK and MCINDOO of these 174 articles was published. Much of the information abstracted relates to tests of DDT insecticides against plant pests under laboratory and small field-plot conditions, but among records of DDT tests against 132 identified species of insects and other arthropods there are notes relating to cockroaches, lice, bedbugs, house and stable flies, ticks, and harvest-mites, of possible medical or hygiene interest. A second list of publications on DDT, designed to bring the bibliography of this subject up to date, and also to call attention to a few older publications that were overlooked

at the time of compiling the first list, appeared in May 1945 (E–660). This second list by ROARK includes a further 418 titles published up to December 31, 1944. *R. L. Sheppard.*

HALL, S. A., SCHECHTER, M. S. & FLECK, E. E. **Chemical Determination of DDT.** *U.S. Bureau Entom. & Plant Quarantine.* 1944, Nov., ET–211, 6 pp., 1 fig. [Processed.] [Summary appears also in *Bulletin of Hygiene.*]

A modification of Winter's method for the determination of halogen in organic compounds (*Indust. & Engin. Chem., Analyt. Ed.*, 1943, v. 15, 571–4) has been adapted to the determination of DDT. About 1 hour is required for an analysis to be carried out, and the method is sufficiently sensitive for the determination of DDT in spray residues. *R. L. Sheppard.*

LWOFF, Marguerite & NICOLLE, P. Recherches sur la nutrition des réduvidés hémophages. IV. Alimentation de *Triatoma infestans* Klug à l'aide de sérum de cheval. Action du glucose. [**The Feeding of** *T. infestans* **with Horse Serum : Action of Glucose.**] *Bull. Soc. Path. Exot.* 1944, v. 37, Nos. 1–2, 38–51, 7 figs.

CH'ING HUA MENG & WINFIELD, G. F. **Studies on the Control of Fecal-borne Diseases in North China. XVIII. An Approach to the Quantitative Study of the House-Frequenting Fly Population. E. The Food Preferences of the Common North China Flies.** *Chinese Med. J.* (Chengtu Edition). 1943, v. 61A, 102–3. [10 refs.] **F. A Preliminary Study of the Life Histories of** *Musca vicina* **Macquart and** *Chrysomyia megacephala* **Fabricius.** *Ibid.* 1943, July, v. 61A, 161–5. [19 refs.]

CH'ING HUA MENG & WINFIELD, G. F. **Studies on the Control of Fecal-borne Diseases in North China. XXVIII–XXXI. Comparative Studies on the House-Frequenting Fly Population of Szechuan, West China. A. The Characteristics of the West China Fly Population.** *Chinese Med. J.* (Chengtu Edition). 1943, Oct., v. 62A, No. 1, 6–11, 1 fig. **B. The Breeding Habits of the Common West China Flies.** *Ibid.* 1944, Jan., v. 62A, No. 2, 71–7. **C. Natural Enemies of the Common West China Flies.** *Ibid.* 1944, Apr., v. 62A, No. 3, 89–92, 1 fig. **D. Life History of** *Sarcophaga fuscicauda* **Bottcher.** *Ibid.* 1944, July, v. 62A, No. 4, 144–9.

TURNER, R. G. **Human Creeping Myiasis. Report of a Case.** *Brit. Med. J.* 1945, July 7, 11–12.

This is an account of a case of myiasis caused by the larva of *Hypoderma bovis*. The patient was a boy, aged 14 years, who lived in London and had never been abroad, but he often went to Epsom Downs. He was admitted to University College Hospital, London, on January 21, 1944, with the following history of his illness. In January 1943, he felt pricking pains over his shoulders and chest which occurred about twice a month until July 1943, when they stopped, but he then noticed, for the first time, a swelling in the skin, about 3 cm. in diameter, painless except that it gave a pricking pain on pressure ; it lasted for 2 days, but similar swellings continued to appear in various parts of the body. They were 1–5 cm. in diameter and were raised 0·5–1 cm. above the surface of the surrounding skin ; they usually remained for a few days and then disappeared. On December 30, 1943, one of these swellings showed a central black spot and, after the application of fomentations, it burst on January 2, and a white maggot appeared after syringing.

On admission to hospital he appeared to be in good health and there were no swellings. His blood was normal except that it contained 22,000 leucocytes per cmm. with 44 per cent. of eosinophils. A swelling appeared on January 24

in the left temporal region and spread round the orbit and across the forehead and remained until February 1. Others followed on various parts of the body; on February 6 a first instar larva of *Hypoderma bovis* was obtained from a swelling and 3 more were obtained during February from other parts of the body. After March 1 there were no more swellings and the patient was discharged on March 10; up to February 22, 1945, there had been no further signs or symptoms.

Human infestation with *H. bovis* has rarely been reported; the author could only find 5 cases in the literature (Herms, "Medical Entomology," p. 342, Macmillan, New York; Miller, *J. Amer. Med. Ass.*, 1910, v. 55, 1978; Smart, *Parasitology*, 1939, v. 31, 130). A case of infestation with *H. lineatum* is reported by Style [this *Bulletin*, 1924, v. 21, 786]. *J. F. Corson.*

Goldman, L. **Pyodermic Myiasis in Children: Observations with special reference to Tórsalo.** *Amer. J. Dis. Children.* 1945, May, v. 69, No. 5, 280–82, 3 figs.

A short note on cutaneous myiasis due to the larva of *Dermatobia hominis*, seen by the author at Tórsalo, Costa Rica [see this *Bulletin*, 1941, v. 38, 351]; photographs of the larva and of *Aëdes angustivittatus*, one of the carriers of the eggs, are shown. *J. F. Corson.*

van den Berghe, L. & Bone, G. Cas de myiase intestinale à *Eristalis*. [**A Case of Intestinal Myiasis due to** *Eristalis*.] *Ann. Soc. Belge de Méd. Trop.* 1944, June 30, v. 24, Nos. 1–2, 69–70, 2 figs. on 1 pl.

LABORATORY PROCEDURES.

Medical Research Council. **The Sterilization, Use and Care of Syringes. By a Committee appointed by the Medical Research Council** [Wilson, G. S., Chairman]. *M.R.C. War Memorandum No. 15.* 23 pp. 8 figs. [44 refs.] 1945. London: H.M. Stationery Office. [4*d.*] [Summary appears also in *Bulletin of Hygiene.*]

There are many records of infections, some serious, caused by therapeutic injections, and these are usually attributable to some fault in aseptic technique. The syringe and needle may be infected owing either to the use of an inefficient method of "sterilization" or to contamination afterwards by fingers, from the air, or by immersion in contaminated water or saline; the injection fluid itself may be contaminated, or the source of infection may be the patient's own skin. This memorandum makes recommendations to guard against all these possibilities, but is concerned chiefly with the first. It is pointed out that the only processes which ensure absolute sterility in a syringe are autoclaving or exposure to a temperature of 160°C. in a dry oven. The cement of glass-metal syringes may melt at these temperatures: the use of all-glass syringes is therefore advocated. These should be enclosed in tubes, the ends of which are tied up with Kraft paper or "Cellophane," and they should preferably be sterilized by dry heat. Boiling is given as an alternative, with the warning that it cannot be depended on to destroy spores: the addition of sodium carbonate to the water will remedy this fault, but "the resulting alkalinity of the syringe may affect drugs or biological products to be injected."

Members of the Committee responsible for this Memorandum conducted experiments themselves from which they conclude that there is no suitable

chemical method of disinfecting an assembled syringe. Immersion in 70–75 per cent. *v/v* alcohol disinfected the separated parts of an all-glass syringe contaminated with staphylococci, but neither those of a glass-metal syringe, nor either type when the alcohol was drawn into the assembled syringe. The use of alcohol is therefore not recommended, except for syringes used only by one patient on himself for administering insulin or adrenaline.

Instructions are also given for the cleaning of syringes, sharpening needles, the conduct of mass inoculations and mass intravenous injections (for which, owing to the risk of transmitting epidemic jaundice a fresh sterile syringe is advocated for each patient), and the pamphlet includes a summary of the precautions necessary for using syringes for certain special purposes. An Appendix reviews the literature on disinfection by alcohol and briefly states the results of the Committee's own observations on this : there is also an account of a method of testing a syringe for leakage. *L. P. Garrod.*

BAUMANN, E. Sterilization und sterile Aufbewahrung von Spritzen und Hohlnadeln. [**The Sterilization and Sterile Preservation of Syringes and Needles.**] *Schweiz. med. Woch.* 1944, Oct. 28, v. 74, No. 43, 1115–33. [27 refs.] [Summary appears also in *Bulletin of Hygiene.*]

This article is the Report of a Commission established by the Union of Swiss Physicians, which has apparently been at work for several years, receiving support from various medical societies, obtaining evidence from them and from many individuals and commercial firms, and undertaking original experimental work. The object of its establishment was to define methods by which infections due to imperfect sterilization of syringes and needles can be prevented, bearing particularly in mind the severe practical difficulties which a high standard of sterility imposes, particularly on the general practitioner. As one member of the Commission remarked : " It is difficult to picture a doctor carrying an autoclave round with him." The report is of great length, and somewhat repetitive and discursive : its 28 sections cover almost every aspect of the subject, including, apart from precautions of all kinds in connexion with the use of syringes, the sterilization of surgical instruments and paraphernalia generally, legal responsibility for septic accidents, war-time difficulties of supply, and the advantages of " Tubunic " ampoules, particularly to mountaineers.

The main conclusions may be summarized as follows. Separate syringes must be kept for injecting sterile medicaments and for aspirating possibly septic material. Different methods are advocated according to whether a syringe has been used for an aseptic purpose or for one which may have contaminated it with pathogenic bacteria ; the processes concerned are referred to as " disinfection " (treatment which will destroy common pathogenic bacteria) and " sterilization " (treatment which will destroy any bacteria whatever, highly resistant spores included). Methods recommended for disinfection are boiling in water, dry heat not pushed to the point of turning cotton wool packing brown, and immersion in the cold in one of three solutions : these consist of 5 per cent. formalin in 70 per cent. alcohol, 5 per cent. " Desogen " (a quaternary ammonium compound) and 1 per cent. sodium nitrite, and a solution containing 2·5 per cent. formalin, 0·5 per cent. phenol, and 1·5 per cent. sodium biborate. Glycerin (1·5 per cent.) may be added to any of these and is said to improve their disinfecting power and prevent jamming of pistons. Sterilization, on the other hand, demands either autoclaving, boiling in a closed vessel under a pressure of 1 atmosphere, dry heat carried to the point of browning cotton wool, or boiling in either 2 per cent. sodium carbonate (with or without the addition of 0·1 per cent. formalin to reinforce disinfectant action, or of 0·1

per cent. sodium nitrite to prevent rusting), or 2 per cent. " Desogen." It is said that traces of these and the foregoing solutions will do no harm to drugs : their possible effect on immunizing agents and on the constituents of blood withdrawn for serological tests does not appear to have been considered.

For much other practical information the original report must be consulted. Two further points of outstanding interest are that the use of alcohol is condemned, and that no preference is expressed for all-glass syringes : glass-metal syringes are obtainable in Switzerland marked " 200°C. " the cement of which does not melt below this temperature. *L. P. Garrod.*

DEMOULIN, M. L. & PARENT, M. Note à propos de la teneur en protides sanguins des Noirs—Réaction de Takata-ara. [**A Note on the Proteins of the Blood in Negroes—the Takata-Ara Reaction.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, Jan., No. 3, 61–6.

The Takata-Ara reaction is said to be related to the ratio of the amount of albumin in the blood to that of globulin ; when the reaction is positive the ratio is less than normal.

The authors made estimations of the blood proteins of African natives of Yangambi, Belgian Congo, and applied the Takata-Ara test to the same sera. The total proteins were precipitated by trichloracetic acid and estimated by the biuret reaction, using a Lovibond colorimeter ; the albumin was estimated in the same way after previous precipitation of globulin by ammonium sulphate. The ratio of albumin to globulin (0·96) was somewhat less than the average ratio (2) found in Europe. The Takata-Ara reaction was positive.

As none of the natives studied had oedema or died of serious liver disease, the authors cannot accept the theory of the production of oedema based on the decrease of the albumin-globulin ratio, nor can they admit that the Takata-Ara reaction has any diagnostic or prognostic value in Africans. *J. F. Corson.*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

MANSON-BAHR, P. **The Manson Saga.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, July, v. 38, No. 6, 401–17. [Refs. in footnotes.] **Other Tributes to Manson's Life and Work.** 417–24. [LOW, G. C. ; HANSCHELL, H. M. ; JAMES, S. P. ; KING, G. ; SCOTT, H. (President).]

The last meeting of the Royal Society of Tropical Medicine and Hygiene held in 1944 was a noteworthy and historic one. It was the birthday of His Majesty the King, who is Patron of the Society, and the meeting was held to celebrate the centenary of the birth of Sir Patrick Manson, Founder and first President of the Society.

Most of the audience had heard parts of the story of Manson's life and career, but none had heard it so completely and so authoritatively delivered as on this occasion by Manson's son-in-law, Sir Philip Manson-Bahr. If we take the usual meaning of Saga—a story of heroic achievement and adventure—we certainly found it here. His discoveries, his achievements, there is no need to dwell on ; every student of tropical medicine knows of them, leprosy, malaria, helminthiasis in man and animals, nematodes, trematodes, cestodes ; trypanosomiasis,

sprue, all were enlightened by his great intellect. As for adventure, what can one think of more adventurous than to carry out, as he did with his brother, a post-mortem examination in a death chamber with a howling mob of fanatical and angry Chinese waiting outside impatiently for their exit, or to attack without waiting; or again, to rob a cemetery at dead of night with a faint light to obtain the larva of a tapeworm? All this many have heard before, but never so fascinatingly described, and, better still, reduced to print for reference so that the gems may be picked out and looked at again and again in the future. The whole is introduced by an excellent reproduction of the oil portrait of Manson by J. Young Hunter. [Might we suggest that more copies of this be produced so that Fellows can procure and frame it without despoiling their copies of the Transactions?]

Sir Philip Manson-Bahr's address was followed by others who had known Manson well: Dr. Carmichael Low, whose association with Manson went back to the last year of the nineteenth century; Dr. Hanschell, who was his house-physician in 1910–11, and kept in close touch with him afterwards. Colonel James, whose personal contact dated from 1907, but who had corresponded with him from India 8 years before. These all gave their personal reminiscences of Manson's career, his personality, his foibles. Of his generous help to the earnest student, of his benefits to medical education they also spoke, and the last point was stressed by Professor Gordon King who told of Manson's influence on medical education in Hong Kong, where his name is perpetuated as the Founder, with Sir James Cantlie, of the Hong Kong College of Medicine. Truly, as the President said at the close of the Session: "Manson has left a memory enshrined and enthroned in the hearts of his many pupils; for such there is no death." *H. Harold Scott.*

SCHWERS, G. A. Les facteurs de la dénatalité au Congo Belge. [**The Causes of Depopulation in the Belgian Congo.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, Jan., No. 3, 43–55.

In the Belgian Congo, anxiety is being felt at the gradual depopulation of certain areas. This depopulation, it is considered, is due to a lowering of the birth rates, and this is evident among some tribes and not among others. One such tribe—the Kundu—which was gradually dying out, was made the object of special study by the author. The results of this study and the theories as to the probable causes of the depopulation are the subject of this article.

Four groups of causes are given. (1) Epidemics, famines, wars, raids, excessive withdrawal of male labour.

(2) Unfavourable "biochemical environment" *e.g.*, poor food giving rise to malnutrition.

(3) Chronic infections, *e.g.*, venereal diseases.

(4) Detribalization and the consequent removal of the control of conduct which tribal rules demanded, and diminishing pride of race.

The author discusses these various causes and, without being didactic, stresses the great importance of the last factor—detribalization.

The idea of the family as a unit has never been recognized by these people. Children belonged to the tribe. The adherence of the individual to the tribal code of behaviour was the guiding rule. When this tribal relationship breaks down, the individual is generally left without any adequate rules of conduct or pride of race. The child, formerly welcomed as a future member of the tribe, is now often unwanted and may even be considered an economic handicap to the mother.

The question is, however, asked—why do some tribes resist social dissolution better than others? To answer this, research, not only by medical scientists but also by those interested in other aspects of the problem, is required.

Mary G. Blacklock.

SEVERENS, J. M. & TANNER, F. W. **The Inheritance of environmentally indueed Characters in Bacteria.** *J. Bacteriology.* 1945, Apr., v. 49; No. 4, 383–93. [27 refs.] [Summary appears also in *Bulletin of Hygiene.*]

Like all populations existing in nature, strains of bacteria are of heterogeneous composition in that individuals are not all exactly alike; therefore, in their investigation of the way in which bacteria become adapted to environmental conditions, the authors used single-cell cultures. The bacteria were *Salmonella pullorum*, *S. schottmülleri* [*Bact. paratyphosum* B] and *Eberthella typhosa* [*Bact. typhosum*], and the results obtained were similar in all three species.

The cultures were incubated for 7 days at 37°C. in broth containing graded concentrations of NaCl, $CuSO_4$, or $HgCl_2$, to determine the highest concentration which permitted growth, this being judged by the presence of turbidity. After this preliminary determination, transplants from single cell cultures were grown in media containing progressively increasing amounts of the respective chemicals; in all cases a marked resistance to the chemical was developed—for NaCl, 2 to 3 times the highest concentration that allowed growth of the non-adapted single cell culture, for $CuSO_4$ it was 4 to 6 times, and for $HgCl_2$, 6 to 12 times. The period of "training" to maximal adaptation (resistance) varied from 69 to 101 days. A comparison with the non-adapted [not exposed to the chemicals] strain was made by plate counts, and it was found that growth of the non-adapted strains was completely inhibited by concentrations which permitted growth of the resistant strains, but the growth of the latter was somewhat retarded by the chemicals. In plain broth the resistant (adapted) and non-resistant (non-adapted) strains grew equally well.

The specificity of the resistance was next investigated, and it was found that a strain adapted to one chemical was not more resistant to either of the other two chemicals than the non-adapted strain was: the resistance, therefore, was specific in the case of these chemicals, but that does not apply, of course, to other substances, such as the sulphonamides, which are more closely related to one another.

Single-cell cultures in plain broth were made from the resistant strains, and their resistance to the particular chemical was tested from time to time; after 18 months' propagation, involving 55 subcultures and thousands of generations, all retained their resistance, hence there was no doubt about the inheritance of the resistant characters. The authors point out that the ability of the resistant bacteria to grow as readily as the non-resistant ones in plain broth assisted the result, since, if they had been unable to grow equally well, even a low rate of reverse mutation [loss of resistance in relatively few bacteria] would soon have produced a population of non-resistant organisms by a process of selection.

The fermentative and morphological characters were unchanged, except that the $CuSO_4$-adapted cells of *S. pullorum* were somewhat elongated.

The mechanism of adaptation.—In this experiment it must be assumed that the resistant forms arose either in response to the action of the chemical, or occurred spontaneously and produced a resistant strain by selective action [the non-resistant bacteria being unable to compete with them in the environment]. The latter possibility was tested by using agar containing a concentration of the respective chemical which inhibited the growth of the non-adapted strain while permitting growth of the adapted strain. This medium was heavily

inoculated with the non-adapted strain and it was found that the strain did contain a few individuals able to grow ; the results are shown in the table.

Organism	No. of colonies on plain agar	No. of colonies on NaCl agar	No. of colonies on $HgCl_2$ agar	No. of colonies on $CuSO_4$ agar
S. pullorum ...	800,000,000	15	21	48
E. typhosa ...	440,000,000	61	32	30
S. schottmülleri	480,000,000	120	16	29

The colonies on the chemical-containing agar were inoculated into broth containing the highest concentration of the chemicals that had been used, and the bacteria grew readily ; a resistant culture was therefore obtained without a long period of " training " to become adapted. It is possible that these few cells had a hereditary mechanism which was susceptible to alteration by the chemical, and the cells became resistant to it because of this after exposure to the chemical. But whether the cells were resistant before exposure to the chemical, or became resistant on exposure to it, it is probable that adaptation of bacteria to various environmental conditions consists of selection of such individuals.

The authors conclude that the bacterial variations described in this experiment are best explained by assuming that they are mutations, a view supported by the specificity and retention of their chemoresistance.

[The question of variation in bacteria and protozoa is of great medical importance and it appears desirable that more work with single-cell cultures and infections should be done.] *J. F. Corson.*

Hodes, P. J. & Keefer, G. P. **Radiology vs. the Monsoon : Effect of Climate upon Equipment.** *Radiology.* 1945, Mar., v. 44, No. 3, 266–72, 8 figs.

This is a useful article, describing in detail the difficulties of diagnostic work in the tropics. The authors appear to have been situated in a valley in India where climatic conditions were exceptionally bad, but their troubles and methods of overcoming them are probably applicable in varying degrees to all tropical areas. They summarize their weather as damp or moist most of the time, uncomfortably hot about half the time, and very dry about one-quarter of the time.

They found that film which had not been tropically packed showed serious fogging, even six to nine months before its expiration date had been reached, while film packed in paraffin-soaked cardboard boxes remained in good condition. Their chief film difficulty was mould, which developed rapidly after processing and disfigured the film in a few days. This can be avoided by placing the film in 5 per cent. formaldehyde for one minute after processing and then drying it slowly in air.

The developing solutions, freshly and properly prepared, were found to be exhausted even before they were used. This was due to organic and inorganic wastes in the water supply and it was not until filtration and settling tanks were added to the water system that this was overcome. Despite these precautions, enough silt still remained in the processing tanks to form a scum which had to be carefully removed. Perspiration dropping on screens was also troublesome until the radiographers had been trained to work rapidly and to open the cassettes only a few inches during loading and unloading.

Bulging of bakelite cassettes was overcome by keeping them dry in a well-ventilated, electrically heated, wooden box. Screen blisters were not infrequent,

but whether they were due to sweat droplets or humidity alone was never determined. Poter-Bucky diaphragms and stationary wafer grids all buckled with the heat, even the lead laminations becoming twisted ; there is apparently no cure for this. Fluoroscopic screens also buckled as the bakelite back warped and allowed moisture in. The authors think, but could not prove, that the luminescence was affected.

Four of eight shock-proof cables broke down, always at the cable terminals, despite weekly applications of special vaseline at the danger points. This was probably due to moisture and to fluctuations in the primary power supply. Corrosion caused trouble from time to time on all switches, meters and contactors, and had to be constantly combated by scraping, sandpapering and repainting, in spite of the fact that thin films of oil were applied frequently to all exposed surfaces. Stainless steel and lead rubber appear to be the only substances unaffected by monsoon conditions. *Peter Kerley.*

Bull. Agric. Congo Belge. 1941, Dec., v. 32, No. 4, 587–639, 2 maps (1 folding). Météorologie du Congo Belge et du Ruanda-Urundi. [**Meteorology of the Belgian Congo and Ruanda-Urundi.**]

BOOK REVIEW.

Gunther, Carl E. M. [M.D., B.S., D.T.M. (Sydney), etc.]. **Practical Malaria Control. A Handbook for Field Workers.** Foreword by Prof. Harvey Sutton, O.B.E., M.D., F.R.A.C.P., B.Sc., D.P.H., F.R.S.I. 91 pp. 1944. New York : Philosophical Library. [15*s.* 6*d.*]

This is not a handbook of malaria control in the ordinary sense in which those words are used. Only thirty of the eighty pages of text are devoted to preventive measures, the remainder of the text consisting of accounts of the clinical signs, diagnosis and treatment of malaria and its complication, blackwater fever. It is written after ten years' experience in New Guinea and is intended for those whose work lies in undeveloped districts with widely scattered populations.

The author describes his opinions as radical. On the subject of malaria control they might be better described as conservative ; he regards the local elimination of malaria as beyond practical reach except in unusual circumstances, and aims rather at the acquisition by Europeans of partial immunity following a reduction in exposure to anophelines by screening and by the siting of dwellings on the lee side of breeding places, with an intervening screen of domestic animals and native people, and by suppression of attacks with prophylactic quinine. The method of collecting mosquito specimens is described, and it is suggested that they should then be sent to some authority for identification and for information on their relation to malaria, breeding habits and the best means of combating them, as personal enquiry on these points demands more time and knowledge than is possessed by the average medical officer. Some measures of control, including the use of fish, the staking of slow rivers, the flushing of streams, the drainage of swamps and the application of oil and Paris green are described, but in no case in sufficient detail to enable the reader to carry out the work without further instruction. An account is given of the screening of houses, and the prophylactic use of quinine is described at length. The author

has had such success with quinine that he has not thought it necessary to look further, and has therefore little experience of atebrin [mepacrine] and plasmoquine [pamaquin].

In the circumstances of the author's practice, there was often little opportunity for the examination of blood films for diagnosis without waste of time which might be dangerous to the patient, and he considers that in the field early diagnosis depends on a thorough understanding of the clinical signs rather than on laboratory aids. The clinical forms of malaria are described in detail, and also laboratory methods. Thick films are condemned on account of the necessity to neutralize the water beforehand, but Leishman's stain (with water freshly neutralized with a lithium carbonate solution, using brom-thymol-blue indicator) is recommended, and the author considers that the ability to perform a reliable leucocyte count is of much more practical value than the more difficult operation of examining a blood film.

The object of treatment is to overcome the immediate attack, and to enable the patient to become "salted" by a subsequent relatively long struggle to maintain control over a chronic infection, rather than to eliminate the parasite from the body. Main reliance is placed on quinine, though courses with atebrin alone and with quinine are described. The combination of atebrin and plasmoquin is condemned as intensely poisonous, and at least 60 per cent. of patients so treated are said to suffer from cyanosis, severe intractable epigastric pains, and extreme mental depression. The section on treatment ends with practical hints on the treatment of malaria in special circumstances, as during pregnancy, lactation, and in children. The book ends with a brief account of blackwater fever.

[The author is right to put forward his own views gained by experience. In many ways they do not coincide with those of the reviewer, who considers that no "handbook for field workers" on "Practical Malaria Control" is complete without a working account of at least one method of preventing infection with the disease other than screening and prophylactic quinine.]

G. Macdonald.

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by The South Essex Recorders, Ltd., Ilford.

(681) Wt. P11/296 11/45 S.E.R. Ltd. Gp. 432

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